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PROCEEDINGS OF INTERNATIONAL SYMPOSIUM ON RECENT
ADVANCES IN THE ASSESSMENT OF THE HEALTH EFFECTS
OF ENVIRONMENTAL POLLUTION, HELD AT PARIS (FRANCE)
ON 24-28 JUNE 1974. VOLUME I

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(LUXEMBOURG)

PREPARED FOR
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EUROPEAN
COMMUNITIES

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PROTECTION AGENCY

WORLD HEALTH
ORGANIZATION

INTERNATIONAL SYMPOSIUM

PROCEEDINGS

Recent Advances in the Assessment of the Health Effects of Environmental Pollution

Volume I

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16. ABSTRACT This publication (in four volumes) contains the full proceedings of this international symposium. It is printed in the original language (Dutch, English, French, German, and Italian) of the individual reports or communications presented, with an English translation of the abstract of each report. The purpose of the meeting was to evaluate the methodologies and techniques available for establishing exposure-effects relationships for environmental pollutants with the goal of encouraging development of sound bases for the establishment of various approaches to protect the public health. These proceedings are made up of more than 250 scientific papers under the broad headings of: The scientific data base required to protect human health, experimental investigations, human effects studies, animal studies, metabolism, interactions, indicators of exposure, population studies, toxicological studies, exposure monitoring, monitoring needs, experimental models, tissue measurements, and environmental measurements. Discussions following papers or groups of papers are also printed. An objective of the symposium was to encourage compatible methodology and data on scientific findings to help ensure that future data will be more directly applicable to the assessment of environmental health effects.		
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DER GESUNDHEITLICHEN FOLGEN DER UMWELTVERSCHMUTZUNG

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VORSLAG
INTERNATIONAAL SYMPOSIUM

RECENTE VORDERINGENBIJ DE VASTSTELLING VAN
DE GEVOLGEN VAN MILIEUVERONTREINIGING VOOR DE GEZONDHEID

Paris (France), June 24-28, 1974

organized jointly by

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PREFACE

Many countries are recognizing the importance of the availability of well established exposure-effect relationships to develop various approaches to protect the public health. This is leading to the use of existing health and monitoring data which in our experience, gained to date, could have been more complete and comparable. To improve this situation the Commission of the European Communities, the United States Environmental Protection Agency and World Health Organization organized in Paris, from 24 to 28 June 1974, an International Symposium on the "Recent Advances in the Assessment of the Health Effects of Environmental Pollution".

The aim of this scientific meeting was to evaluate the methodologies and techniques currently available for establishing exposure-effect relationships for environmental pollutants. The subject matter covered by the Symposium emphasized three main areas which could offer approaches to a more common denominator in methodology. Hopefully, wide acceptance of such a denominator will help to ensure that future data will be more directly applicable to an assessment of the nature, role, and significance of health effects.

Hopefully this contribution will be useful for establishing appropriate environmental control plans to prevent or reduce adverse health effects, from exposure to environmental pollutants.

on behalf of the Organizing Committee,

D.H. DIETERICH (WHO) S.M. GREENFIELD (EPA) P. RECHT (CEC)

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EDITORIAL NOTE

This presentation contains the full proceedings of the Symposium. Volumes I and IV include the broad coverage papers presented at plenary sessions as well as all panel discussions; and the opening and closing sessions which set forth essentially the intent and conclusions of the Symposium respectively. Volumes II and III contain all papers presented at specialized sessions as well as the supplementary reports.

The reports and communications are published in their original language Dutch, English, French, German, and Italian, with an English translation of the abstracts. The opening and closing sessions are published in the original language and English. We wish to point out that the views expressed in the various communications are the responsibility of the authors and may or may not represent the views of their sponsors. Through our extensive editing, and rearrangement of the order of the presentations we have produced a shorter and hopefully more readable document.

We anticipate that these proceedings will be a valuable contribution to the necessary exchange of scientific knowledge, to the enhancement of human health, and to the protection of the environment.

BERLIN, ENGEL, SWEETS

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Simone VEIL - Ministre de la Santé (France)

OPENING ADDRESS

DR. RUSSELL W. PETERSON

Chairman President's Council on Environmental Quality
United States of America

I wish to express, on behalf of the United States' delegation, our appreciation for being able to work with all of you in this Symposium, which promises to be helpful to all of us.

During the next five days, we shall be dealing with a wide range of research areas related to man's health and the environment to which his health is so intimately bound. In arranging for the present series of meetings, the Commission of the European Communities, the World Health Organization, and the U.S. Environmental Protection Agency have brought together an eminent group of scientists from the fields of medicine, chemistry, toxicology, epidemiology, physics, engineering, and mathematics. This spectrum of disciplines in itself gives some indication of the vast resources and many factors we must bring to bear on developing truly effective programs to protect health and enhance our environmental quality.

Let us for a moment place some of these factors in perspective, because they will surely impinge upon our discussions this week. Certainly any viable environmental protection program must be predicated on several components. One of the most basic of these relates to the promulgation of a firm body of environmentally protective guides, laws, or codes. Sound legislation or protective guidelines, based on thorough knowledge, should enable us to assure that the protection of the health and welfare of our citizens is given full scope within the entire range of our activities. Science can contribute much to the development of our environmental codes by expanding our knowledge of the impact man exerts on ecological systems and the effects which this impact in turn exerts upon man.

Authority to direct environmental protection efforts or programs must be vested in a responsible and responsive agent. Much has been said and written about the global nature of environmental pollution, and I believe we are all realizing that any one institution charged with environmental concerns cannot limit itself to the problems within its own geographical boundaries. Its decisions should be based upon balanced considerations, insofar as possible, of a myriad of national and world-wide, direct and indirect, consequences of any one action.

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Our experience in the U.S. continues to reveal that the choices are not easy. We are becoming progressively aware, for example, of the need to evaluate the total health, social, and economic effects of available options for controlling pollution prior to their selection as the measure of choice. Similarly, in this time of dwindling energy supplies, we all face the task of meeting our world-wide energy requirements while insuring that public health is protected from potential adverse effects of energy production; this requires that as we seek expanded and alternative energy technologies, we exercise prudence lest we trade an energy crisis for a health crisis.

A third component we must consider is the attitudes of society toward environmentally protective measures. In any decision-making process, the public should be informed of the need for and rationale behind a given action. Thus broadly speaking, we must ultimately include in our deliberations the extent to which society is willing to pit the risks of pollution against the benefits of an ever-growing world-wide technology. The benefits are usually widely proclaimed. This is not normally the case with risks. Modern man is barraged with a variety of health insults - the risks of some are evident, the risks of others can be estimated, but the risks remain unknown to us.

In the case of air pollutants, for example, early evidence suggested that health risks were associated with exposure to sulfur dioxide. We now have sufficient information to postulate that these risks stem more directly from exposure to sulfate compounds produced by atmospheric conversion of sulfur dioxide than to the sulfur dioxide itself, and we can even make some predictions about potential exposure levels from various stationary and mobile air pollution sources.

On the other hand, the precise, reproducible methods necessary for monitoring exposure to and quantifying the risks from certain air pollutants, notably nitrogen oxides, remain to be established. Further, there exists a variety of other substances, not nearly as widely studied as the major air pollutants, which are suspected as toxicants but for which we lack adequate information to assess health risks. A case in point relates to the carcinogenic properties of vinyl chloride recently observed under conditions of occupational exposure in the U.S. We have only meagre data on the health effects of this substance under a very particular set of circumstances and virtually little data on its non-occupational implications.

We are thus confronted with some fundamental questions about whether to regulate or control a number of materials, to what levels we need to reduce their presence, and how to best control those materials which have been identified as posing a known risk to public health. Setting standards, establishing regulations, issuing protection guides, or other similar forms of

national and world-wide decisions require that we possess technically adequate and defensible data. So that rational environmental and technological choices can be made, then, we must obtain knowledge about the known risks associated with each alternative open to us, the risks we can reasonably estimate, the benefits of our actions, and the areas where our data are insufficient for appropriate action. Because only a concerted research effort can provide this information, the scientific aspect of any environmental protection program should be considered an underlying and most essential component.

This of course places a tremendous burden of responsibility on the scientific community. It is imperative, therefore, that we as scientists develop means of obtaining technical information which are comparable, that we develop experimental approaches and methodologies on which we agree. But what are some of the areas where we most critically need to formulate common approaches? In assembling data on any given class of pollutants, we need to measure the levels of pollution emanating from the source or sources we have identified. We need to monitor human exposure and be able to estimate incremental exposures with time if the source were to remain uncontrolled. To do this, we need sampling and measurement techniques which are valid and reproducible not only within the same laboratory but between the laboratories using these techniques. We need comparable systems and techniques for monitoring exposures as well as predictive models which are equivalent. By the same token, we need analogous methods to determine the environmental transport and possible transformations of the pollutants in question, their effects on ecosystems, and, most importantly, their impact on human health.

Perhaps at this point we might do well to ask ourselves, "What should health intelligence assess?" We should certainly consider how best to define susceptible populations, the validity of employing animal studies to predict human health effects, and what kinds of indicators are most sensitive for determining human health effects. We should also consider how best to study effects associated with an extended period of latency, with an extended low level of exposure, or with subclinical manifestations. Inherent in our assessment must be an awareness of the need to determine an adequate, but not excessive, margin of safety for the establishment of prudent health protection guides.

Over the next few days, we shall be discussing such topics as the health implications of exposure to noise, to pollutants resulting from fossil fuel combustion, to pesticides, and to other materials pervading the environment. Our fundamental objective in studies of this nature is to determine exposure and to discern exposure-effect relationships. Herein lies the essence of the contribution we as scientists must provide for successful environmental protection programs and where we must concentrate our attempts at achieving comparable results. We will inevitably come to grips with the concept of threshold

limits. We shall consider factors shaping the dose-response curve, such as age and nutritional status of the subject, intercurrent disease, duration, level, route, and method of exposure, as well as the proper application of statistics. We will also come to grips with the validity of experimental design for studying the possibly non-threshold effects of pollutants such as those which are carcinogenic, mutagenic, or teratogenic, and whether the experimental design reflects the actual conditions of use or exposure.

I am certain that specific points of disagreement on many of the subjects I have mentioned will surface, but constructive controversy is desirable. Only by communicating with one another on our areas of scientific discord can we resolve them, both on a national and an international scale. I would like to add that I am optimistic about the attempts to achieve standardization of methods and inter-laboratory quality assurance which are already underway within and among a number of nations. The air monitoring program of WHO is certainly a substantive effort in this direction. In addition, the development of the WHO Environmental Health Criteria Documents should prove to be of real value in fostering the collaborative accumulation of research information, the interpretation of data, and the identification of gap areas in our knowledge. Whether we are affiliated with the academic, industrial, or governmental sectors, we can all benefit from these efforts. I would urge that such programs be strongly supported and extended to include as many laboratories from as many nations as possible.

I believe that the present conference, with its emphasis on comparable approaches for discerning exposure-effect relationships, will prove to be another major step in promoting the mutual scientific understanding we critically require for effective health protection programs. I look forward to our collective deliberations.

OPENING ADDRESS

DR. P. J. HILLERY

Vice-President of the Commission of the European Communities

It is a great pleasure for me, on behalf of the Commission of the European Communities - one of the co-organizers - to welcome you to this international symposium

The fact that so many prominent personalities in this field have decided to attend is not only a great honour for the organizing Committee and the Commission, but it also underlines the considerable interest there is in the problems involved in the theme of this symposium which is devoted to the protection of public health against environmental pollution.

We are also extremely pleased that so many other international organizations, as well as experts from nearly 50 countries, are present. This demonstrates the world-wide interest there is in studying and exchanging views on the scope of the problems involved and in gathering together useful information and scientific data.

I would like to extend a special welcome to the representatives of the other European Community Institutions. The fact that the European Parliament and Economic and Social Committee are represented at this symposium is a cause of considerable encouragement to the Commission.

Indeed the interest of the European Community in the problems of the environment was underlined by the Council of Ministers' decision on 19 July 1973 to establish an environmental action programme.

Various activities in this field have since been developed and a number of practical measures have already been undertaken with the aim of reducing environmental pollution, increasing health protection and improving the quality of people's lives.

Since its inception in 1958, the European Community has achieved a substantial increase in the rate of economic growth, which has literally transformed the life and face of Western Europe and brought to the great majority of its people higher living standards and wider horizons.

However, this greater prosperity has not resolved all the problems. On the contrary, it has exacerbated some and created

new ones also. There are now problems caused by growth itself: problems of industrial pollution, of a deteriorating environment, of a conflict of values - in some cases between industry and society - disruptions to the pattern of life, and many others.

Unless these problems can be resolved, economic growth will fail to provide the quality of life which people rightly expect. The aim of the European Communities' environmental policy, and of the Communities' Social Action Programme is to improve the conditions in which people of our countries live and work.

To reach this desirable goal, it is essential that, as a first step, scientific criteria be drawn up based on adequate information, so that we have common reference data for the elaboration of programmes and standards for the protection of man and his environment. The knowledge of such factors as the observed effects on human health of exposure to various pollutants is essential to an objective evaluation of the environmental risks involved in any particular undertaking or work process.

It goes without saying that the approach to such studies should be scientific and that conclusions should be based on proven facts. Only in this way will it be possible to make the precise assessments of the nature, and significance of the health effects of pollutants.

Without going too deeply into the various interests concerned in programmes to protect man's environment, I would say that considering the risks to public health involved in pollution and considering the benefits to be derived from the application of scientific preventive measures, there is an indispensable need for close collaboration between scientists, economists and political leaders.

To tackle effectively problems of such a large scale at regional or national level is nowadays virtually impossible. To attempt it would be a waste of effort, energy and finance. International collaboration is needed. For this reason we welcome the multi-national nature of this conference organized by three co-sponsors of very different background.

This congress, where more than 250 papers will be presented in more than 10 plenary and parallel sessions is structured in such a way that a very broad scientific field is covered. We realise that the meeting by itself is not a panacea. The problems are too complicated and the many existing local and regional situations differ greatly whether considered from an industrial, ecological, social, demographic or economic point of view.

But we all agree that there is sufficient common ground for many of the problems and many useful lessons that can be drawn from the pooling of information and experience.

Much has changed since the first international congress on public health was held in 1851. Since that time there has been an exponential growth in scientific information and fundamental methods of research have been developed to include not only deductive analysis but also inductive experimental techniques, especially in the new discipline of toxicology.

Exchanges of views between scientists and the conclusions drawn by them in their publications and meetings can now have a very great impact on political discussions. It is therefore essential that the work of scientists be concerned with critical analysis so that the competent authorities can take decisions on the basis of solid research and advice.

A special effort will, I trust, be made during this meeting to achieve a better comprehension of the mechanisms and parameters of pollution and its effects on public health. If this target is attained, then this Symposium can be considered a success. In this context I might refer to the very successful colloquium "Environmental Health Aspects of Lead" organized by the European Communities in collaboration with the United States Environmental Protection Agency, which was held in Amsterdam nearly two years ago. In recent scientific literature reference is very often made to both the proceedings and the papers of that Symposium. This should encourage new efforts.

Before ending, I would also like to thank on behalf of the Commission, the other co-sponsors of this Symposium - the United States Environmental Protection Agency, and the World Health Organization with its headquarters in Geneva and its regional office in Copenhagen - for their co-operation during the preparation of this congress. I have been informed that despite the great geographical separation of the three organizations and all the administrative complications arising from this, the preparatory work has been done in an atmosphere of friendly and close co-operation. We are very grateful for this.

I would also like to express my thanks to the Director General of the Unesco and his collaborators for allowing the use of this splendid congress building and also for helping us with the necessary preparations.

In conclusion, I should like to express the hope that this Symposium will not only be a scientific but also a human success, and that all who have to take decisions concerning the protection of man and his environment will draw useful lessons and information from these discussions which will help them to carry out their responsibilities in the best interests of mankind.

OPENING ADDRESS

DR. T. ADEOYE LAMBO

Deputy Director-General, World Health Organization

It is with great pleasure that, on behalf of Dr. Mahler, Director-General of the World Health Organization, I address this distinguished gathering of scientists and health workers who will discuss during this week one of the most important aspects of the relationship of the environment to man's health.

The mere fact that more than 900 participants from about 50 countries are attending this Symposium, organized jointly by the Commission of the European Communities, the United States Environmental Protection Agency and the World Health Organization, shows the increasing awareness of the medical and health profession, the scientific community and the public at large of the need to improve the quality of the environment in which we live and work.

The promotion of environmental health is one of the constitutional obligations of the World Health Organization. The WHO Constitution, adopted by the International Health Conference held in New York in 1946, stipulates that the function of the organization is, inter alia, "to promote, in cooperation with other specialized agencies where necessary, the improvement of nutrition, housing, sanitation, recreation, economic or working conditions and other aspects of environmental hygiene" and "to promote cooperation among scientific and professional groups which contribute to the advancement of health".

The subject of the Symposium belongs to the most important aspects of environmental health because the assessment of health-effects of environmental pollution and other hazards is one of the primary criteria on which governments should base their policies and decisions related to environmental control. These decisions must be based on the best available scientific knowledge and not on the prevailing political atmosphere or emotional reaction of the public, because they involve expenditure of public funds of enormous magnitude.

I should like to give you only one example to illustrate this point. A WHO study presented to the Twenty-fifth World Health Assembly in 1972 revealed that in 1970, 1258 million people in 90 selected developing countries did not have an adequate community water supply, and that by 1980 this will increase to 1781 million, unless adequate measures are taken.

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To reach the target set by the World Health Assembly for the Second Development Decade. i.e. that 60% of urban dwellers should be served by house connexions and 40% by public stand points, and that 25% of the rural population should have reasonable access to safe water, the total average annual investment required will be of the order of US \$ 1.3 billion.

Safe community water supply is, of course, only one element of the total environmental quality improvement; other elements such as waste management, air pollution control, food safety, improvement of housing and recreational conditions, require annual investments which are in some instances even higher than the one mentioned in this example. The decision on how much should be done to improve environmental conditions, obviously requires as sound a scientific basis as it is possible to have at a given time, and the major component of this basis is the quantitative relationship between the level of exposure to environmental hazards and the resulting effects on health and ecosystems.

Although this Symposium will deal only with one specialized aspect of environmental health, that is with health effects of environmental pollutants - and quite rightly so in order to enable in-depth and critical examination of this problem - I should like to point out that the World Health Organization looks at environmental quality problems in a much wider context in agreement with the definition on which the WHO constitution is based, that "health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity."

In view of this, I feel it necessary to stress the need for a holistic and ecological approach in social and health action to improve the human environment and underline the importance for human health and man's well-being of all aspects of the human environment, physical, chemical and biological as well as psychosocial and socio-economic factors; and the increasing awareness that psychosocial factors, as well as the bio-physical ones, can precipitate or counteract physical and mental ill health, profoundly modify the outcome of health action and influence the general quality of life.

Since bio-physical factors, such as environmental pollutants, will be extensively discussed during this Symposium, I should not like to take your time in describing the direct influence they may have on human health. It seems to me more appropriate to point out that socio-economic and psychosocial influences, such as poverty, affluence, population growth, mobility of populations, urbanization, psychosocial stress and the cultural environment can profoundly modify the effects of environmental pollution and other bio-physical factors. In other words, there is a synergistic relationship between these two sets of factors. Failure

to consider various interactions of environmental factors, such as the effects of other pollutants, smoking, alcohol, various drugs and industrial or agricultural chemical exposures has been common. Moreover, environmental pollutants should be considered to be not only primary toxicants but also modifiers or co-factors of natural diseases. In view of this complex relationship, it is imperative to have the full participation of many disciplines in many of these programmes.

There is evidence, for example, that the effects of air pollution can be promoted by concomitant climatological conditions, socio-economic factors, stress situations and smoking habits. Besides well-defined effects, such as the deterioration of respiratory function or incidental peaks in mortality and morbidity during disastrous accumulations of pollutants in a prolonged inversion period, there is evidence that chronic exposure to low levels of atmospheric pollutants may be a factor in non-specific respiratory disease, and may cause interference with bodily functions, detriment of performance and, as suggested by animal experimentation, premature ageing. Because of this, the results of environmental pollution studies should be carefully evaluated as to their possible interaction with biasing influences. There is a great need for a multi-dimensional prediction model of the status of health and physiological functions in relation to race, sex, age, climate, geography, nutrition, smoking and other habits and living conditions.

Smoking cigarettes, i.e. the inhalation of cigarette smoke, is a most important factor producing disease per se and in preparing the respiratory tract, and probably other systems in the body to react unfavourably to noxious gases, vapours and particulates. There is evidence that in the case of certain types of exposure to asbestos, miner's bronchitis and the respiratory function of iron and steel-foundry workers, the moderate smoker already has an increased risk. He is less able to cope with the superimposed impact of atmospheric pollutants upon the respiratory organs. Smoking habits should be carefully taken into account not only when planning and performing air pollution research, but also in the evaluation of the epidemiological and experimental results.

To a considerable extent geography, topography and local climate determine the fate of pollutants. This is essentially true for changes in the temperature gradient of the atmosphere, which can lead to the accumulation of air pollutants over a number of hours or days. Persistent pollutants such as mercury, cadmium and some organochlorine compounds may appear in several environmental media (air, water, soil, food) and may reach man through a variety of environmental pathways; they may accumulate in the environment or may change their physical state and chemical form; they may also be metabolized in micro-organisms and higher plants or animals, producing sometimes more toxic compounds.

Water that is drained from polluted land may become harmful if used as drinking water for animals or man. This is increasingly so in urbanized and industrialized areas with a high water demand. Some air pollutants may contaminate surface waters and, in some instances, increase the background concentration of certain toxic substances causing, as a result of accumulation, an adverse ecological condition; fluorine and arsenic are well-known examples.

Pollution of the marine environment is another concern because of its implications for health (use for recreational purposes, marine food products), but there are many other aspects of this problem (ecological and economic) which are of great importance.

In order to determine the effects on human health, human beings have to be studied. Extrapolation of results on animals to human beings has limited applicability. Studies on human volunteers are limited by the duration and magnitude of exposures that can be ethically used. Because of this, advantage must be taken of those situations where human populations are exposed to various levels and combinations of pollutants. Epidemiological studies are used to evaluate such exposures.

Criteria for environmental quality for the protection of human health must depend on information that defines the limits of concentration of environmental pollution which permit maintenance of normal growth, structure and function. Such criteria are often derived from experimental studies on animals and, when possible, on human volunteers. Another source is from experiences in industry. Whatever the source, the information must be unequivocal as to its reliability and relevance to exposures of human beings to pollutants. This has not characterized much of the past experimental data.

The insidious adverse effects of environmental factors, such as carcinogenic, teratogenic and mutagenic effects, that may result from long-term environmental exposure are at present of greater social concern than the acute or subacute effects because of a far greater uncertainty about the chronic adverse effects. There is a strong pressure therefore, for a preventive approach through predictions and evaluations of such effects before human data on such effects have been obtained.

Health effects also to be considered are those that have a bearing on the general well-being of man but without clear evidence of disease, at least as evaluated by methods now available. The response may often consist of only a feeling of discomfort and annoyance. It is not known at present what is meant by "annoyance" and what bearing it has on human health in the long run. A number of persons who report that they are annoyed also report other effects such as disturbances of sleep, headache or nausea. This complex and ill-defined emotional and behavioural reaction

may cause sensitive or vulnerable persons to develop a psychosomatic disorder or may aggravate existing diseases. There is an urgent need to study this further.

To facilitate the international comparisons of data necessary to the solution of many of the problems of environmental health, it is essential that investigators use standardized techniques and scientific methodology of proven validity and that the findings should be presented uniformly.

Economic and ecological effects of pollution must be taken into consideration to assess the total effect on man. They include effects on weather, vegetation, domestic and wild animals, damage to aquatic and other food resources, destruction of materials, as well as soiling and impairment of aesthetic values and recreational amenities resulting in an economic loss to man; their appraisal is an essential prerequisite for setting up of environmental quality standards and for regulatory control of pollution.

In addition, the cost to society of controlling pollution must be determined and then compared to the benefits resulting from its control, and risks to health arising from inadequate control. The degree of health protection desired above the acceptable minimum level (which at the very least should assure protection from death and illness directly resulting from exposure to pollution) is a matter of political decision and is generally purchased at increasing increments in control costs; these costs are also directly related to the deadline by which the control is to be achieved; the shorter the time deadline, the higher are the costs. The level of protection desired depends, of course, on the type and severity of health effects and the size of population involved, but other factors (social, cultural and economic) and other health priorities must be considered as well.

As the Director-General of WHO very recently reported to the World Health Assembly, health oriented environmental pollution control programmes differ from the traditional medical and public health programmes, and the relevant policy formulation is a new challenge because it involves not only science, technology, legislation and administrative enforcement, but also economic policy as related to energy production and use, industrial structure, land use, national and international trade, consumption, and conservation of natural resources; and finally problems of damages and compensation, allocation of costs and fiscal problems of taxes and charges.

These are only a few of the problems encountered in the assessment of health effects of environmental pollutants and its administrative uses. I have no doubt that this week's deliberations will make most valuable contributions to the elucidation

of some of these questions, and thus provide a better scientific basis for those who have to make decisions on measures to be taken to prevent or control environmental hazards.

May I conclude by wishing you great success in your meeting this week.

DISCOURS INAUGURAL

DR. RENE MAHEU

Directeur Général Unesco

(présenté par M. le Dr. M. Batisse)

Le Directeur Général de l'Unesco, M. René Maheu, appelé dans une autre salle par les travaux de notre Conseil Exécutif qui se réunit en ce moment, regrette de n'avoir pu assister à cette séance d'ouverture. Il m'a prié de l'excuser auprès de vous et de vous accueillir ici en son nom.

Il m'est particulièrement agréable de souhaiter la bienvenue dans cette maison aux éminents spécialistes qui, sur l'invitation de trois organisations avec lesquelles l'Unesco entretient des relations étroites s'apprêtent à examiner les progrès récents dans l'évaluation des effets de la pollution de l'environnement sur la santé.

Ce sujet particulier n'est pas de ceux auxquels l'Unesco apporte par son action une contribution directe puisque, dans le système des Nations Unies, les problèmes d'ordre sanitaire sont par définition du ressort de l'Organisation Mondiale de la Santé. Mais ce n'est pas pour autant un sujet auquel l'Unesco peut rester indifférente, car tout se tient lorsqu'il s'agit d'environnement, de développement économique et social, du devenir de l'homme sur notre planète devenue trop étroite.

Aussi ne me paraît-il pas inutile de rappeler ici brièvement les grandes lignes ainsi que certains traits de l'action de l'Unesco en matière d'environnement, et de souligner combien vos préoccupations et les nôtres peuvent être complémentaires dans ce vaste domaine.

Pour l'Unesco, l'environnement de l'homme est constitué non seulement par l'ensemble des facteurs et des situations physiques et biologiques qui influencent sa vie, mais aussi par les conditions sociales et culturelles diverses dans lesquelles il se trouve. C'est donc un concept très large qui comporte à la fois des éléments objectifs et subjectifs, et qui s'étend du cadre de vie journalier dans la maison ou l'agglomération jusqu'au plan régional et global des interactions entre l'homme et la nature.

Face à un sujet aussi vaste, l'Unesco a entrepris, dès sa fondation, différentes activités qui, au cours des vingt-cinq dernières années, se sont déployées surtout dans le domaine des sciences naturelles. Cependant il est apparu peu à peu nécessaire de réserver, dans les entreprises de recherche et de formation scientifiques relatives aux ressources naturelles et à l'environnement, une part de plus en plus grande aux facteurs proprement humains; en d'autres termes, il s'agit désormais d'accroître la contribution des sciences sociales, des sciences du comportement et de l'éducation.

Cette évolution est déjà sensible dans le cas du programme intergouvernemental et interdisciplinaire sur l'homme et la biosphère (MAB). Ce programme de coopération scientifique, qui offre aux Etats membres la possibilité d'examiner en commun des problèmes concrets, constitue à l'heure actuelle l'élément prépondérant des activités de l'Unesco relatives à l'environnement. Il est dirigé par un Conseil international de coordination auquel siègent les représentants de 25 pays et ceux des principales organisations internationales compétentes, en particulier l'OMS. Il s'appuie sur des comités nationaux - il en existe 70 à l'heure actuelle - chargés d'assurer la participation des pays aux projets internationaux du MAB qui les intéressent.

Ces projets internationaux visent, d'une manière générale, à déterminer les interactions entre l'homme et les grands écosystèmes qui constituent la biosphère, de façon à assurer à la fois l'utilisation la plus judicieuse possible des ressources et la protection des intérêts à long terme de l'humanité. Ils sont consacrés notamment à l'étude des effets écologiques des activités humaines sur les écosystèmes des forêts tropicales sur les terres à pâturage, ou sur les systèmes insulaires ou montagneux, et ils examinent en même temps certains processus à l'intérieur de ces systèmes tels que les conséquences écologiques de l'utilisation des pesticides et des engrais, ou les interactions entre la transformation de l'environnement et l'évolution démographique et génétique. Parmi les projets du MAB, il en est un qui vise à créer un réseau mondial de zones protégées, les "réserves de la biosphère", qui pourraient être utilisées non seulement pour la protection des espèces qu'elles contiennent, mais aussi comme zones témoins et comme zones d'expérimentation sur les effets de la pollution générale des écosystèmes et sur la surveillance continue de cette pollution.

Parallèlement à ce programme interdisciplinaire sur l'homme et la biosphère qui est centré sur une méthode écologique, l'Unesco poursuit deux autres grands programmes scientifiques qu'il convient de mentionner ici consacrés respectivement à l'eau et à la mer. Pour ce qui est de l'eau, la décennie hydrologique internationale, lancée en 1965 et axée principalement sur la compréhension, l'évaluation quantitative et l'utilisation rationnelle des ressources en eau, va prendre fin cette année.

Elle sera suivie, dès 1975, par un programme hydrologique international où l'accent sera mis davantage sur les aspects qualitatifs, notamment sur la pollution des eaux et sur l'influence de l'homme sur les ressources hydriques. Dans le domaine des sciences de la mer, l'Unesco assure le Secrétariat de la Commission océanographique intergouvernementale et s'attache à promouvoir un ensemble d'activités d'observation, de recherche et de formation permettant d'étudier et de mesurer la pollution des océans ou de mieux comprendre les systèmes océaniques et les problèmes des régions côtières. Ces programmes internationaux de recherche sur les interactions entre les activités humaines et le fonctionnement ainsi que l'évolution des grands systèmes de la nature, qu'il s'agisse des terres, des eaux ou des mers, m'ont paru devoir être évoqués en cette circonstance car ils ont pour objet le cadre naturel d'ensemble dans lequel se placent les effets particuliers sur la santé de l'homme qui sont ceux qui vous intéressent.

Mais ce n'est pas, je crois, notre seul point de contact. Il en existe au moins deux autres : la qualité de la vie et l'éducation.

Ce qu'on désigne par les mots "la qualité de la vie" est sans doute encore mal défini et comporte bien des éléments susceptibles d'interprétations et d'appréciations subjectives diverses. Mais il y a aussi des éléments objectifs très importants, au premier rang desquels ceux qui ont trait à la santé et qui vont fournir la matière de vos travaux. En tout cas on ne saurait douter de l'importance croissante que les questions en cause, sous leurs différents aspects, assument dans l'opinion. En fait, c'est là sans doute avec le sous-développement le plus grand sujet d'anxiété pour la conscience humaine présente. Ce qu'on appelle crise de l'environnement est, en effet, essentiellement un aspect d'une crise de civilisation fondée, d'une part sur les craintes que l'homme éprouve pour la survie de l'espèce en raison de son comportement aberrant à l'égard de la nature et de ses ressources et, d'autre part, sur l'insatisfaction spirituelle sur laquelle débouche le mode de vie qu'il s'est donné. Et cette crise est particulièrement marquée dans les agglomérations urbaines sans cesse plus monstrueuses où l'homme semble à proprement parler se "dénaturer" et devenir étranger à lui-même.

C'est pourquoi l'Unesco a entrepris de stimuler et coordonner un effort de réflexion, de recherche et de discussion en vue de mieux comprendre l'environnement immédiat de l'homme et promouvoir une meilleure conception du cadre de vie et de l'habitat. Dans ce domaine, la perception de la qualité de l'environnement, les facteurs psychologiques, sociologiques et culturels, les fondements du comportement individuel et collectif deviennent essentiels à l'orientation de l'action publique et rejoignent, me semble-t-il, les préoccupations qui vous animent aujourd'hui en ce qui concerne la santé de l'homme.

En même temps nous atteignons ici une autre dimension de l'action, tout aussi essentielle: celle de l'éducation. L'amélioration des relations entre l'homme et la nature, qui est indispensable au développement harmonieux de l'individu et des sociétés, exige, en effet, une meilleure compréhension des interactions qui sont à la base des systèmes dont dépendent la vie et l'épanouissement de l'homme. Pour sa part, l'Unesco s'emploie à favoriser cette éducation à tous les niveaux, qu'il s'agisse d'enseignement scolaire ou d'éducation des adultes, de la formation avancée d'écologistes ou de la refonte de l'enseignement donné aux architectes, aux urbanistes et, surtout, aux ingénieurs, qui sans doute apparaissent comme de grands perturbateurs de l'environnement, mais qui peuvent aussi, grâce aux conclusions de travaux comme les vôtres et les nôtres, apporter des remèdes à la situation présente.

Ces quelques indications sur les activités de l'Unesco en matière d'environnement auront suffi, je l'espère, à vous montrer l'intérêt que nous attachons aux résultats de votre réunion. De la réalité ou de la gravité des dangers que les diverses pollutions constituent pour la santé de l'homme et que vous allez devoir évaluer dépend, en effet, pour une large part, la nature et l'étendue des mesures qui devront être prises, ce qui ne manquera pas d'influer sur le programme de l'Organisation. Nous vous demandons donc de considérer cette maison comme la vôtre et vous souhaitons le plus grand succès dans vos travaux.

OPENING ADDRESS *(translation)*

DR. RENE MAHEU

Director-General, Unesco

(presented by Dr. M. Batisse)

The Director-General of Unesco, Mr. René Maheu, has been called to attend a meeting of our Executive Board. He is sorry he is unable to be present at this opening session and has asked me to convey his apologies and welcome you on his behalf.

It is an especial pleasure for me to welcome here today the eminent specialists who, at the invitation of three organizations with which Unesco maintains close contact, are to examine recent progress in evaluating the health effects of environmental pollution.

Strictly speaking, Unesco does not act directly in this area since, by definition, within the United Nations system health problems are the responsibility of the World Health Organization. Yet Unesco cannot remain indifferent, for where the environment is concerned, economic and social development and the very future of man on this increasingly crowded planet are at stake.

I therefore feel that in this context it would be worthwhile for me to run over the basic principles and some specific aspects of Unesco action in the environmental field, and to show how much, in this vast area, your concerns and ours are often complementary.

Unesco considers man's environment to consist not only of all the physical and biological factors and situations which affect our lives, but also of the various social and cultural conditions which surround us. The concept is thus a very broad one with both subjective and objective elements extending from everyday life in the home or town to interaction between man and nature at the regional and global level.

Confronted with such an extensive field, Unesco has since its inception, initiated various activities which, over the last 25 years, have been mainly concerned with the natural sciences. However, it has become increasingly clear that research and scientific training establishments concerned with natural

resources and the environment should concentrate more and more on specifically human factors - in other words, from now on we should see that the social and behavioural sciences and education play a greater part.

This trend can already be seen in the intergovernmental interdisciplinary programme on "Man and the Biosphere" (MAB). This scientific cooperation project enabling Member States to examine concrete problems jointly is the most important of Unesco's environmental activities at the present time. It is directed by an international coordinating council consisting of representatives from 25 countries as well as from the WHO and the other major international organizations concerned. It is backed up by national committees - of which there are now 70 - responsible for ensuring that countries take part in the international MAB projects which are of interest to them.

Generally speaking, the aim of these international projects is to determine the interaction between man and the major ecosystems which constitute the biosphere, with a view to ensuring the most judicious use of resources together with the protection of humanity's long-term interests. They concern the study of the ecological effects of human activities on the ecosystems in tropical forests, grazing lands and mountainous or insular systems, as well as the examination of certain processes within these systems such as the ecological consequences of the use of pesticides and fertilizers or the interaction between changes in the environment and demographic and genetic trends. One of the MAB projects is aimed at creating a world network of protected areas or "biosphere reserves" which could be used both for the protection of the species within them and as control and experimental zones for studying and continuously monitoring the overall effects of the pollution of ecosystems.

Side by side with this interdisciplinary programme which examines man and the biosphere from the ecological viewpoint, Unesco has two other major scientific programmes worthy of mention here. One is concerned with fresh water, the other with the sea. The International Hydrological Decade which started in 1965 and is mainly concerned with the understanding, quantitative evaluation and rational use of fresh water resources, is to end this year. In 1975 it will be followed by an International Hydrological Programme which will focus on the qualitative aspects, particularly water pollution and man's influence on water resources. In the area of the marine sciences Unesco provides the Secretariat for the Intergovernmental Oceanographic Commission and seeks to promote a combination of observation, research and training activities for studying and measuring marine pollution and for improving knowledge of oceanic systems and problems in coastal areas.

I felt it important on this occasion to mention these international research programmes on the interaction between human activities and the workings of and changes in the major natural systems whether on land, in fresh water or in the sea, their subject is the overall natural framework which contains the specific effects of pollution on human health in which you are interested.

However, it seems to me that apart from this, we have at least two other points of contact - the quality of life and education.

It may well be that "the quality of life" has not yet been properly defined - it certainly covers many aspects giving rise to varying subjective interpretations and evaluations. Yet there are also some extremely important objective aspects including, at the top of the list, the health considerations on which your work is to be based. In any event, there is no doubt that public opinion is showing increasing concern for the various aspects of the problems in question. Indeed, together with underdevelopment, this is probably the subject which is now the greatest burden on man's conscience. What is known as the environmental crisis is, in fact, basically one aspect of a civilization crisis which has arisen, on the one hand from man's fears about the survival of the species as a result of his aberrant behaviour towards nature and natural resources, and, on the other hand, from his spiritual dissatisfaction derived from the way of life he has created for himself. The crisis is particularly apparent in the ever more monstrous urban areas where man really seems to be "denaturing" himself and losing his true identity.

This is why Unesco has undertaken this effort to stimulate and coordinate thought, research and discussion with a view to gaining a better understanding of man's immediate environment and helping design a better setting and habitat for our lives. In this field, appreciation of the quality of the environment, psychological, sociological and cultural factors, and the motives of individual and collective behaviour are becoming essential to the guidance of public action, and, I believe, link up with the issues which concern you today on the subject of human health.

This brings us to another, equally vital aspect of our action - education. Improved relations between man and nature so essential to the harmonious development of the individual and of societies - are in fact dependent on a better understanding of the interactions underlying the systems on which man's life and development depend. For its part, Unesco strives to promote such education at all levels, whether it be through schools, adult education, the advanced training of ecologists, or through a new conception of the training of architects, urbanists and,

above all, engineers who doubtless appear as major perturbers of the environment, but who could also remedy the present state of affairs by taking note of the conclusions drawn from work such as yours and ours.

These few indications about Unesco activities in the environmental field will, I think, convince you of our interest in the results of your meeting. The nature and extent of the measures adopted will depend to a large extent on the existence or gravity of the various pollution hazards to human health which you are about to evaluate. This analysis will no doubt influence our Organization's programme.

We hope you will feel at home here and we wish you every success in your work.

DISCOURS INAUGURAL

SIMONE VEIL

Ministre de la Santé - France

Les dégradations subies par l'environnement du fait des transformations du monde moderne et les risques que cette situation fait encourir à la santé des populations, constituent l'un des principaux sujets de préoccupation de notre époque.

Depuis le début du siècle, les pouvoirs publics avaient orienté de manière prioritaire leur action vers les aspects bactériologiques de la pollution du milieu naturel, et poursuivi notamment la lutte contre les grandes endémies, telles que le choléra ou la fièvre typhoïde. A cet égard, du fait du développement de la vaccination et de l'hygiène, ainsi que des mesures d'assainissement prises contre les vecteurs des maladies, rongeurs ou insectes, des progrès considérables ont pu être réalisés, même si, depuis peu, de nouvelles inquiétudes se font jour, en raison de facteurs récents tels que la résistance accrue de certains microbes aux antibiotiques ou le développement des voyages intercontinentaux.

Or, depuis à peu près une trentaine d'années, la pollution de l'environnement ne cesse de s'accroître dans les sociétés industrialisées et cet état de fait constitue pour la santé des êtres humains une menace de plus en plus redoutable. Il est dès à présent certain, en effet, que nombreux et graves sont les troubles qui sont liés à la dégradation du milieu, qu'il s'agisse de la pollution de l'air, de l'eau, des produits alimentaires ou encore de l'effet du bruit, ou de l'action des micro-polluants, rencontrés dans ses différents milieux.

Les raisons de cette situation sont à présent bien connues et font déjà l'objet de larges discussions dans l'opinion publique. Elles tiennent essentiellement à cinq grandes causes: le rejet d'énormes quantités de substances toxiques par certaines industries, l'utilisation massive en agriculture de multiples produits chimiques, et notamment des engrais et des pesticides, le surpeuplement de quelques grands centres urbains dans lesquels se trouvent concentrées des centaines de milliers de personnes, la circulation intensive des véhicules individuels dans les villes et enfin l'innovation technologique qui fait apparaître sur le marché, chaque année, 400 à 500 substances chimiques nouvelles dont il est rarement possible de prévoir toutes les conséquences éventuelles sur la santé de la population.

Deux tentations, dès lors, se font jour. Celle de l'immobilisme qui tendrait à entraver systématiquement tout nouveau progrès technique de peur de nouvelles nuisances, et celle, au contraire, du fatalisme, qui inciterait à s'en remettre à la providence, ou aux découvertes futures de la médecine, du soin de compenser toutes les conséquences négatives pour la santé publique des transformations de notre société.

Ces deux attitudes sont également excessives. La première aurait conduit, au milieu du siècle dernier, à ne jamais creuser un tunnel de chemin de fer pour éviter aux voyageurs le risque de périr étouffés. La seconde, conjuguée avec une confiance aveugle dans la technique, peut mener à certains désastres tels que ceux de Minamata ou de la Thalidomide.

Or, l'état d'esprit qui doit animer les milieux scientifiques et les responsables politiques des divers pays est tout autre. Il s'agit en effet, à présent, de considérer avec objectivité et réalisme, et en substituant la rigueur et la précision scientifique à l'irrationnalité des impressions et des angoisses, ce problème majeur des risques pour la santé du fait de l'environnement. La réunion de votre symposium manifeste avec tout l'éclat désirable notre volonté commune d'aboutir à ce résultat.

Incontestablement, la situation en matière de maladies et de troubles dus à la dégradation du milieu naturel est préoccupante.

La pollution de l'air, provoquée par l'action conjuguée de l'industrie, du chauffage en milieu urbain, des rejets de substances toxiques par les véhicules automobiles et de l'incinération des déchets, entraîne dans certaines ères géographiques une agression pulmonaire dont les conséquences peuvent être particulièrement redoutables. Il semble en effet qu'il y ait une corrélation étroite entre la pollution atmosphérique et certaines maladies des bronches, et en particulier l'emphysème pulmonaire et le cancer du poumon. Chacun se souvient, par exemple, du smog de Londres de 1952 qui a provoqué près de 5.000 décès en une semaine du fait de l'aggravation subite de maladies cardiaques et respiratoires.

La pollution de l'eau est à peine moins redoutable. Provoquée aussi bien par l'excessive concentration urbaine que par le rejet de déchets industriels, elle peut entraîner des intoxications aiguës et des maladies chroniques du fait de certains éléments micro-polluants, tels que les hydrocarbures, les pesticides ou les détergents, dont les effets peuvent ne s'avérer toxiques qu'après plusieurs années d'absorption d'eau polluée.

Cependant la dégradation de la qualité de l'air et de l'eau ne sont pas les seuls sujets de préoccupation en matière de santé publique. Certaines substances, répandues dans tout notre environnement - l'eau, l'air et les aliments - constituent également un péril redoutable, qu'il s'agisse de l'amiante, du plomb, du mercure, du cadmium, du dioxyde de soufre, ou des pesticides organophosphorés dont la toxicité peut se trouver multipliée par l'effet de phénomènes de synergie encore mal connus. A ces divers éléments de pollution d'autres facteurs viennent s'ajouter, tel que notamment le bruit, qui dans certaines circonstances peut diminuer l'acuité auditive et atteindre l'équilibre nerveux de l'homme, c'est-à-dire le diminuer et le dégrader.

C'est pourquoi, après une longue période de temps où il semblait que les découvertes de la médecine n'allaient plus cesser de faire progresser l'espérance de vie des hommes, l'inquiétude à nouveau grandit.

La tâche à laquelle seront consacrés les travaux de votre symposium est donc d'une importance capitale. Elle est aussi, nous le savons tous, d'une extrême difficulté.

L'incidence nocive de la pollution de l'environnement sur la santé humaine est à présent incontestable. Particulièrement significatif est à cet égard ce passage d'une communication de savants américains de l'université de Cleveland qui déclarent "il y a maintenant peu de doute que beaucoup de maladies chroniques, jusqu'à présent considérées comme spontanées, et en particulier le cancer, sont provoquées par des polluants de l'environnement". Mais si, globalement, la toxicité de la pollution est indéniable il s'agit d'un phénomène tellement impalpable dans la multiplicité de ses manifestations, aussi bien en ce qui concerne les agents polluants que les personnes atteintes dans leur santé, que les problèmes posés aux autorités scientifiques sont d'une complexité à peine imaginable. Pour ne prendre que le seul exemple de l'eau, combien de difficultés à résoudre, qu'il s'agisse de la détection rapide de pollutions accidentelles, de la contamination des eaux souterraines, du conditionnement des eaux de table ou du développement de certaines maladies comme l'hépatite virale ...

Cette tâche gigantesque, vous l'accomplissez, dans vos spécialités respectives, par les méthodes scientifiques les plus variées, de la recherche fondamentale à la recherche appliquée, de l'envergure des enquêtes en matière d'épidémiologie à la poursuite de l'infiniment petit pour la détection des substances les plus fines, du questionnaire à l'examen somatique, et des expériences réalisées sur les animaux aux études consacrées notamment en milieu hospitalier, à l'étiologie probable des divers troubles affectant les malades. Ce symposium doit permettre à présent d'opérer une confrontation générale du résultat de toutes ces recherches.

Je crois, à cet égard, important de souligner tout l'intérêt qui s'attache à une harmonisation plus complète des données scientifiques en matière de pollution et de répercussion sur la santé. Qu'il s'agisse notamment des protocoles opératoires des enquêtes épidémiologiques, des méthodes de mesure des paramètres de la pollution ou du choix des types de population retenus pour l'étude d'un phénomène, il est en effet essentiel que tous les milieux scientifiques intéressés s'accordent à utiliser les mêmes définitions et les mêmes instruments de mesure afin que leurs travaux puissent aboutir à des résultats parfaitement clairs et non contestés.

L'objectif suprême de toutes ces études si diversifiées consiste évidemment dans la possibilité de déterminer en toute connaissance de cause des normes précises pour réglementer l'utilisation des substances polluantes, détecter les accidents ou les abus possibles, et les sanctionner s'il y a lieu.

Il y a bien longtemps que les pouvoirs publics se préoccupent de ces problèmes puisqu'en matière de pollution de l'eau et de l'air, les premières mesures importantes sur le plan juridique remontent en France au tout début du siècle et que nombreux sont les textes législatifs et réglementaires qui sont intervenus surtout depuis une quinzaine d'années dans le domaine de la protection de l'environnement. Mais il faut aller encore beaucoup plus loin, et notamment améliorer l'étendue, la fiabilité et l'automatisation des réseaux de contrôle pour aboutir aux réseaux de surveillance globale de l'environnement recommandés par la conférence des Nations-Unies tenue en 1972 à Stockholm. C'est en ce sens que s'orientent les pouvoirs publics français qui ont mis en oeuvre à Rouen un réseau continu de mesure de la pollution atmosphérique qui va être également installé à Fos-sur-Mer, en vue de déclancher une éventuelle alerte.

On conçoit aisément que l'ensemble de cette réglementation pose un nombre considérable de problèmes techniques notamment en ce qui concerne la constatation du caractère polluant de certains produits et leur détection dans le milieu ambiant. Il se pose également des problèmes juridiques, dans la mesure où il faut fixer des normes et les sanctionner, et aussi de problèmes économiques, puisqu'aussi bien la mise en place de dispositifs antipolluants peut dans bien des cas grever plus ou moins lourdement le coût de certains produits. Toutes ces difficultés ne peuvent être résolues qu'au prix d'une collaboration étroite entre les milieux de la recherche scientifique, les administrations et professions touchant au domaine de la santé, plusieurs départements ministériels, et en particulier l'environnement, l'industrie et l'agriculture, et aussi, et plus encore peut-être, la population dans son ensemble.

Dans ce domaine capital du choix entre d'une part, l'accélération sans limite du progrès technologique - avec ses conséquences bénéfiques sur la progression du niveau de vie de l'ensemble des citoyens et ses "retombées" néfastes pour leur santé - et d'autre part, le contrôle ainsi que, le cas échéant, la limitation de cette évolution dans un souci de prudence, il est essentiel que l'opinion soit complètement informée de tous les éléments du problème et décider du genre de solution qui lui paraît le plus opportun. L'éducation, l'information, la discussion, la persuasion me paraissent en effet des arguments beaucoup plus décisifs que la contrainte. Si l'hygiène corporelle, par exemple, est un facteur essentiel de la santé d'une population, mieux vaut évidemment en persuader l'ensemble des citoyens que de vouloir en ce domaine contrôler tout un chacun et sanctionner la carence des plus négligents ...

Les autorités de santé publique ont, pour leur part, un rôle primordial à remplir dans l'élaboration et la mise en oeuvre d'un programme rationnel de lutte contre les nouvelles agressions du monde moderne. Les données médicales, dans la mesure où elles sont susceptibles de protéger la santé de l'être humain contre les agressions multiples de l'environnement, doivent en effet prendre le pas sur toutes les autres considérations.

Dans la définition d'une politique de sauvegarde de l'environnement, les autorités sanitaires constituent certainement "l'interlocuteur privilégié" des services mis en place pour assurer la coordination des actions entreprises en ce domaine. C'est dans cette optique que le Ministère français de la santé a entrepris, conformément aux indications de l'Organisation Mondiale de la Santé, de restructurer ses services d'hygiène publique. En outre l'Institut National de la Santé et de la Recherche Médicale consacre une part importante de ses activités à des études sur les conséquences de la dégradation de l'environnement sur la santé.

Telles sont quelques unes des observations que je tenais à présenter à l'ouverture de ce symposium, en ma qualité de Ministre Français de la Santé. Je ne doute pas qu'il ne contribue puissamment à faire plus de lumière sur des problèmes que nous avons encore beaucoup de peine à appréhender dans toute l'étendue de leur complexité. Plus tard, sans doute, sera-t-il possible d'évaluer de manière plus précise le coût économique de la lutte à mener sur tous les fronts contre la pollution de milieu naturel et aussi de déterminer au terme de débats publics particulièrement approfondis - une notion de risque acceptable en matière d'environnement comparable à celle qui est déjà retenue, au moins de manière implicite, en matière de vaccination obligatoire.

Aussi les préoccupations qui sont les nôtres ne doivent-elles en aucun cas nous inciter au pessimisme. A partir du moment, en effet, où l'ensemble de la population prend conscience du péril que représente pour elle la dégradation du milieu ambiant, cette évolution des esprits autorise les plus grands espoirs. Ainsi, déjà, dans notre pays, des rivières totalement polluées ont-elles pu permettre à nouveau le retour de la vie animale et végétale, les produits non bio-dégradables ont-ils été presque totalement interdits dans les détergents, et des réglementations plus protectrices sont en cours d'élaboration dans plusieurs domaines importants relevant de la Santé Publique et de l'Environnement.

Dans cette gigantesque bataille engagée pour la protection de l'être humain contre les menaces multiples de son cadre de vie, vos travaux vont apporter une contribution de tout premier plan. Car beaucoup, nous le savons tous, reste à faire, pour que la planète terre qui constitue - avec sa mince couche d'humus et son fragile vernis de civilisation - notre seule chance de survie, ne soit plus considérée comme une immense carrière ouverte à toutes les convoitises, mais qu'elle devienne enfin, pleinement et définitivement, la terre des hommes.

OPENING ADDRESS

SIMONE VEIL (translation)
Minister of Health - France

One of the major causes of concern to the present generation is the deterioration of the environment as a result of modern industrial development and the health hazards to which the population is consequently exposed.

Since the beginning of the century, public authorities have given priority to the bacteriological aspects of pollution of the natural environment, and have emphasized control of the main endemic diseases such as cholera of typhoid. Significant progress has been made in this field through the development of vaccination, improvements in hygiene and campaigns against disease carriers such as rodents or insects, though of late further problems have arisen as a result of new factors such as the increased resistance of certain microbes to antibiotics or the growth of intercontinental travel.

For some thirty years, environmental pollution has been growing steadily in industrialized societies, and this situation poses an increasingly grave threat to the health of human beings. Indeed it is already established that many serious effects are associated with the deterioration of the environment in its various forms: air and water pollution, contamination of food-stuffs, the effects of noise or the action of micropollutants.

The reasons for this situation are now well known and are already the subject of a wide-ranging public debate. There are five main causes: disposal of huge quantities of toxic substances by certain industries, massive use in agriculture of numerous chemical products, especially fertilizers and pesticides, overpopulation of a number of large urban centres in which hundreds of thousands of people are concentrated, heavy private traffic in towns, and finally technological progress, which introduces each year on the market four to five hundred new chemical products, whose possible effects on the health of the population can rarely be foreseen.

Two temptations now arise. The first is the temptation to freeze all action, consistently blocking all technical progress for fear of creating new sources of pollution. The second is the temptation to adopt a fatalistic approach, to rely on providence or on future medical discoveries to counteract all the negative effects on public health of the development of our society.

Both attitudes are extreme. Had the first been current in the middle of the last century, no railway tunnels would have been driven lest passengers died of suffocation. The second, in combination with blind trust in technology, can lead to disasters such as Minamata or thalidomide.

Scientific circles, however, and politicians exercising responsibility in the different countries should tackle the matter in a very different frame of mind. An objective and realistic approach replacing irrational impressions and fears by the discipline and precision of science must now be adopted to the major problem of environmental health hazards. This symposium is a dramatic assertion that it is our common purpose to achieve this end.

The situation with regard to illnesses and disorders caused by deterioration of the natural environment undoubtedly gives cause for concern.

In certain geographic areas, air pollution resulting from the combined effects of industry, urban heating, toxic emissions by motor vehicles and waste incineration leads to pulmonary effects with particularly serious consequences. There appears to be a close correlation between atmospheric pollution and certain bronchial diseases, especially emphysema and lung cancer. Who, for example, does not remember the London smog of 1952 which caused nearly 5,000 deaths in one week as a result of the aggravation of heart and respiratory diseases?

Water pollution is scarcely less serious. It is caused both by excessive urbanization and by the discharge of industrial waste, and can lead to acute poisoning and chronic illnesses through the action of certain micropollutants, such as hydrocarbons, pesticides or detergents, the toxic effects of which may not become apparent until polluted water has been absorbed over a period of years.

Deterioration of air and water quality, however, are not the only public health problems. Certain substances dispersed throughout our environment - in water, air and foodstuffs - also pose a grave threat. They include asbestos, lead, mercury, cadmium, sulphur dioxide and organo-phosphate pesticides, the toxicity of which may be multiplied by as yet unknown synergic effects. In addition to these various pollutants, there are other factors, such as noise, which in certain circumstances may lead to impaired hearing and affect the nervous balance by upsetting and damaging the human nervous system.

For all these reasons anxiety is again increasing after a long period in which it seemed that medical discoveries would continue indefinitely to improve life expectation.

The task to which this symposium is devoted is therefore of vital importance, but as we are all well aware, it is also very difficult.

It cannot now be denied that environmental pollution has a harmful effect on human health. In this connection the following passage from a statement by American scientists from the University of Cleveland is of particular significance: "There is now little doubt that many chronic illnesses, especially cancer, which until now were thought to develop spontaneously, are caused by environmental pollutants." But while in general terms the toxic effects of pollution are undeniable, the phenomenon is so elusive and appears in so many forms both as regards the pollutants and the persons affected that the scientific authorities are faced with problems whose complexity can scarcely be imagined. To take water alone as an example, how many difficulties must be overcome, whether these lie in the rapid detection of accidental pollution, contamination of subterranean water, treatment of drinking water or the development of certain diseases such as virulent hepatitis.

This is an enormous task, which you accomplish in your respective fields by the most varied scientific methods ranging from pure to applied research, from large scale investigations in epidemiology to highly detailed work on the detection of trace substances from the questionnaire to somatic examination, and from experiments on animals to studies devoted, in clinical surroundings, to the determination of the probable etiology of the various symptoms affecting victims of disease. The purpose of the present symposium is the general confrontation of all these research activities.

I should like at this point to emphasize the importance of fuller harmonization of scientific data regarding pollution and its effects on health. Whether we consider case reports in epidemiological inquiries, methods of monitoring pollution parameters or the choice of population groups for the study of a particular phenomenon, it is essential that all scientific bodies concerned agree on common definitions and common measuring instruments so that the results of their studies may be absolutely clear and beyond dispute.

The ultimate aim of this whole range of studies is obviously to have a basis of knowledge on which to establish precise standards allowing the use of pollutants to be controlled, accidents and any violations of regulations to be detected and sanctions imposed where appropriate.

The public authorities have long been concerned with these problems, and the first major legal measures in France with regard to air and water pollution date from the very beginning of the century, while numerous laws and regulations concerning environmental protection have been promulgated, especially in the last fifteen years. Much more remains to be done, however, especially improving the comprehensiveness, reliability and automation of monitoring systems with a view to establishing the type of global environmental monitoring system recommended by the 1972 United Nations conference in Stockholm. The French authorities are moving in this direction by establishing at Rouen a continuous monitoring network for atmospheric pollution. The same system will also be set up at Fos-sur-Mer to give the alert if necessary.

It will be readily appreciated that this corpus of legislation raises a large number of technical problems especially determining that certain products are pollutants and detecting them in the environment.

It also poses legal problems, as standards have to be set and enforced, and economic problems, as the installation of pollution control plant frequently affects the cost of certain products to varying degrees. All these difficulties can be solved only if there is close cooperation between the scientific research community, the administrative services and professions concerned with health, several government departments, especially the Departments of the Environment, Industry and Agriculture, and most important of all perhaps, the population as a whole.

Now that we are faced with this crucial choice between unchecked acceleration of technological progress - with its beneficial effect in improving the standard of living and its harmful "fall-out" affecting health - and surveillance and if necessary restriction of this development as a precautionary measure, it is essential for the public to be fully aware of all aspects of the problem and to choose the form of solution it finds most suitable. Education, information, discussion and persuasion seem to me more effective than compulsion. If, for example, personal hygiene is a major factor affecting the health of a population, it is obviously better to convince all the citizens of its necessity than to attempt to check each individual and punish the worst offenders.

The public health authorities have a central role to play in devising and implementing a rational programme to control the new hazards arising in the modern world. Insofar as they protect health against the numerous environmental insults, medical requirements must take precedence over all other considerations.

In drawing up an environment policy, the health authorities must certainly have a "special relationship" with the departments set up to coordinate all action in this field. This is the approach which the French Ministry of Health has adopted in reorganizing the public health departments in accordance with the recommendations of the World Health Organization. The National Institute of Health and Medical Research moreover, devotes much of its energies to investigating the effects on health of environmental pollution.

These, are a few of the points which, as French Minister of Health, I felt I ought to raise by way of opening this symposium. I am sure this assembly will make a major contribution to elucidating problems which are still difficult to grasp in all their complexity. At a later date it will no doubt be possible to arrive at a more precise estimate of the economic cost of the war to be waged on all fronts against pollution of the natural environment and also to define after the fullest public debate the concept of an acceptable degree of risk in environmental matters similar to that already applied, at least implicitly, in the field of compulsory vaccination.

The problems with which we are concerned thus give no grounds for pessimism. Indeed, if the population as a whole becomes aware of the danger to which it is exposed through pollution of the environment, this evolution of attitudes is justification for the very highest hopes. In France for example, animal and vegetable life has already returned to rivers which were totally polluted, virtually all use of non-biodegradable products in detergents has been prohibited, and in several areas under the responsibility of Health and Environment regulations designed to afford a higher degree of protection are being drafted.

Your work will play a vitally important role in this vast battle to protect the human being against the multifarious threats posed by the world around him. As we are all well aware, much is still to be done before the planet Earth, which - with its fine layer of humus and its thin veneer of civilization - is our only hope of survival, is no longer regarded as a huge quarry to be exploited for the satisfaction of every form of greed but becomes, in the fullest sense, the home-land of mankind.

POPULATIONSUNTERSUCHUNGEN
POPULATION STUDIES
ETUDES SUR LA POPULATION
STUDI SULLA POPOLAZIONE
BEVOLKINGSSTUDIES

Vorsitzender - Chairman - Président - Presidente - Voorzitter

D. RALL (U.S.A.)

*Stellvertretender Vorsitzender - Vice Chairman - Vice-président
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W. GOERKE
(Bundesrepublik Deutschland)

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THE EFFECT OF ENVIRONMENTAL FACTORS ON HEALTH -
METHODS FOR POPULATION STUDIES

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ABSTRACT

The paper deals with the epidemiological methods and sources of information which are useful for the investigation of the influence of environmental factors on health. Suggestions are made for developments in identification of new health hazards and of monitoring the health of population groups.

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As we all know, there are various techniques that can be used to study the effect of environmental factors on the health of the population. Certain information, such as the nature of the condition under investigation, how frequently it occurs and who it is most likely to affect, must be considered when a study is being designed so that the most appropriate technique can be chosen.

When a specific environmental factor can be isolated, its effect on health can be detected relatively simply. In the studies of the development of cancer of the lung in asbestos and nickel workers (Doll [1] ; Newhouse [2]), for example, the investigators knew that they were dealing with a specific industrial process which had been used in the manufacture of these substances for many years. Cancer of the lung is a relatively rare condition and in order to establish its incidence in the population at risk it is necessary to study either very large population groups or small groups of individuals exposed for a very long period of time. Furthermore, since the condition is uniformly fatal, it is sufficient to identify individuals who die rather than those who develop symptoms. In these particular studies, therefore, the number of years a given industrial population was at risk from either asbestos or nickel and how many cases of cancer of the lung had occurred were calculated and compared with the incidence of cancer of the lung in the general population over the same time period. Results showed that the risk of developing lung cancer was very much greater in both asbestos and nickel workers than in the population as a whole. One assumption made in this study was that the smoking habits of these workers were similar to those of the population at large. However, as the excess risks were high this was unlikely to have changed the outcome substantially.

In most investigations of environmental health hazards, however, the picture is obscured by the variety of factors involved. The general techniques that are currently used by epidemiologists in such investigations follow classical lines.

A clue to the need for investigation is often first found in published statistical information, perhaps by examining mortality ratios for people in different industries, living in different towns or regions, or from different social class or economic groups. This may be followed by scrutiny of morbidity or illness statistics and although the

quality of this type of data varies greatly, it may help to form precise hypotheses. It creates the possibility, for example, of examining hospital discharge rates for different areas, or sickness absence rates in a particular industry or for those living in a particular region or town. Disability or early retirement rates are usually available for the working population and can provide crude evidence of a health hazard related to the working environment.

Let us now, however, consider the far more common way in which one undertakes a study, namely the investigation of the prevalence or incidence of a condition in a defined population. In any population the frequency of disease at any moment in time depends on the rate of inception, recovery and recurrence and on mortality among those afflicted by it. As it is inception that is the most relevant in epidemiological studies of cause of disease, records are considered of prime value because they reflect the onset of the disease. Too often, however, such data are either absent or inadequate and the only alternative is a survey of the current prevalence of disease within the community.

Prevalence studies are designed to estimate the number of people with a particular disorder of defined severity in a population at one point in time. In practice this means the number counted not at any one point in time but over a certain short period. The first step then is to define the population to be studied. A possible difficulty here is the choice of area and this will, of course, depend on the particular hazard to be investigated. Some years ago, for example, we were interested in determining the influence of air pollution on the aetiology of chronic bronchitis. The best way to answer this question would obviously have been to investigate random samples of the population from areas with different levels of pollution. However, since we knew that social class and occupational factors influenced the onset of this condition, we would have had to look at very large numbers of individuals in each area to be able to exclude their possible effects on differences in prevalence. To avoid this difficulty, we chose individuals in the same occupation, which was not liable to be at risk from chronic bronchitis, and examined all those following this occupation in two areas. We thus standardised for exposure to occupational hazards and social class, and were able to identify the

effect of two independent factors, namely cigarette smoking and level of air pollution (Holland and Reid [3]).

A further difficulty in the choice of a population is that it is necessary to examine individuals who have been exposed to the environmental factor under investigation for a known period of time. And here migration may interfere. If an area is prone to contamination from a particular health hazard, it is likely that people will move away - and it may be that the most susceptible will move. Studies by Bradford Hill [4] among others have shown that migrants from an area differ in susceptibility and resistance to disease from those who remain. It is thus important to have some idea of the differential rate of migration of individuals exposed or not exposed to a particular hazard. In industrial studies this is relatively easy since the records of a particular industry in terms of premature death and retirement of workers can be obtained.

It is also possible, in looking at environmental hazards, to use a population of children. They tend to remain in the same area at least for a certain known period of time and, since they usually go to school near their homes, it is relatively easy to determine the effect of an environmental factor.

In comparisons of different groups of the population exposed to environmental hazards, it is also important to choose appropriate control groups. In considering an environmental hazard in an industry, for example, it is possible to examine illness or morbidity amongst husbands and wives, using the wives as controls. It is unlikely that they will be exposed to the same occupational hazards as their husbands whereas both are likely to be exposed to the same environmental hazard.

Whatever population is chosen, it is important to investigate that population as completely as possible. Information on those who do not participate is essential - they may, for example, have refused because they are ill or because they fear the consequence of having the disease discovered.

Having defined the population and decided what variables to measure, the next step is to collect the necessary information. One method of doing this is by questionnaire. This is usually better than a clinical history which may not identify and record in a repeatable

way what the individual actually says. The importance of using a standardised questionnaire, such as that developed by the EEC and the MRC on chronic bronchitis, has been amply demonstrated. But whatever questionnaire is used, it is vital that the sensitivity, specificity and precision of the individual questions are validated (Cochrane and Holland 5). And interviewing techniques must also be standardised.

Physiological tests are another method of obtaining the necessary information. Such tests must be simple and if possible cheap to administer, acceptable to those who receive them, and must produce accurate and repeatable results. They must also be 'sensitive' (give a positive finding in those who have the condition under investigation) and 'specific' (give a negative finding in those who do not have the condition under investigation). Those who administer the tests must be trained, equipment standardised, and factors such as the time of day and season of the year recorded as these may affect the results considerably.

These then are the basic criteria for the prevalence or retrospective investigations which are commonly used to estimate the relative risk of a particular health hazard. Incidence or longitudinal investigations, which are obviously much more expensive to carry out, are appropriate when the absolute risk must be ascertained.

So far, I have discussed the standard epidemiological techniques used in population studies throughout the world. Let us now, for a moment, look towards the future and consider some of the possible techniques.

The first such technique which, in my view, merits serious consideration is tracer index case or rare event analysis. Various situations in the recent past have emphasised the importance of identifying a rare event - perhaps the best known example is the thalidomide tragedy. We must equip ourselves to recognise harmful new agents in the environment so that these can be removed or immobilised before too much damage is caused. It is difficult to visualise how such an epidemiological method could be put into effective practice. One possibility would be for various international agencies to collect information on specific conditions and identify suspicious clustering of cases. Examples of this type of monitoring exist already in the World Health Organisation and in the Office of

Population Censuses and Surveys in the area of congenital malformation. But this is not sufficient and further possibilities to extend this technique must be explored.

The monitoring of events in society, is another technique which requires development. Sophisticated methods exist for the surveillance of infectious diseases such as malaria and smallpox and these have proved their worth. However, we have not yet gone far enough in trying to monitor changes in chronic disease brought about by alterations in the normal environment. The difficulty with this, of course, is the time aspect - the diseases which are common nowadays take many years to develop. For the development of such a technique, therefore, it is necessary to begin to think of tracer elements or changes in function or symptoms rather than the full-blown developments of the disease itself. One example of this type of monitoring is our study of the surveillance of growth in schoolchildren to see whether entry into the EEC and changes in social welfare policy, such as the provision of free school milk, have any effect on their nutrition (6). Again I would suggest that much research needs to be done in this area in future years.

Finally, may I make a plea for more attention to be paid to analysis of disease and symptom complexes. We are now adding vast numbers of chemicals to our water supply and yet we know little if anything about the possible effects of health. Since it is unlikely that these will necessarily produce changes in the pattern of known diseases, we must be able to assess the occurrence of new diseases and symptoms. Thus a recent printout of the analysis of the water supply in London revealed the presence of considerable numbers of chemicals, admittedly in very minute quantities. In future we may be able to control our population with greater ease than at present but perhaps they will all be sterile!

In this talk I have tried to give a brief outline of current standard methods of studying the effects of environmental factors on health and to suggest some possible areas for future development. This is a difficult and complex field where issues are clouded by economic and political considerations which cannot be ignored. But if we are to cope successfully with this increasingly important area of health, we must equip ourselves with more sensitive, sophisticated and flexible methods of collecting the evidence.

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DISCUSSION

CARNOW (U.S.A.)

The rates of disease were less in the American cohort than the urban or rural U.K. group. What U.S. group was studied and how do you account for the difference?

HOLLAND (U.K.)

We studied male A.T. & T. van drivers aged 40 - 59 in three U.S. cities. We examined 96 - 98% of all men classified as drivers in the three cities. The reason for the difference was probably that levels of air pollution were lower in the U.S. cities than in the three English country towns.

HOUSEHOLD SURVEY OF THE INCIDENCE OF RESPIRATORY DISEASE IN RELATION TO ENVIRONMENTAL POLLUTANTS

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ABSTRACT

A study was undertaken to determine the incidence of respiratory disease in households in a midwestern suburban middle-class community, in a relatively unpolluted area. The sample included 441 families, divided into two groups; those utilizing gas cookery and those utilizing electric cookery. Family health and demographic data were obtained from the participants. The period of the study was one year. Reports of acute respiratory illness were obtained through bi-weekly telephone calls to each of the households. The respondents were asked to report respiratory illness in any member of the household, and to indicate the presence or absence of a set of signs and symptoms. Ambient air was analyzed, indoors and outdoors, in a sample of the households, and pulmonary function tests were conducted on a 42 percent sample of the participants, representing both types of household.

The results of the study are presented with regard to reported incidence of respiratory illness in the two types of household. AID analysis and multiple regression were carried out to determine the best set of independent variables as predictors of respiratory disease incidence. This is the first

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in a series of studies. Subsequent studies will follow-up the reported respiratory illness to ascertain objective signs of illness and obtain bacterial cultures. Similar studies are also contemplated in areas in which the ambient air is more heavily polluted.

1. Introduction

In the combustion of fossil fuels, many substances are produced that are toxic at certain concentrations. A substance of particular interest is NO_2 . Although it is known that NO_2 may be fatal to persons exposed to high concentrations, such as 500 ppm that may be encountered in silos, very little is known about long-term exposure to low levels of concentration. Recent studies in Chattanooga [1,2,3] indicated that persons living in areas with elevated levels of ambient NO_2 , reported a high incidence of respiratory illness. This caused some concern regarding the possible effects of NO_2 on the incidence of respiratory illness. It is known that the open flame in gas ranges can produce short-term elevation of NO_2 concentration in the cooking area. However, the possible effects on the respiratory health of members of such households have not been assessed adequately. Accordingly, the present study was initiated to acquire data for making such assessments.

In the Chattanooga area, it was found that in addition to the NO_2 , there were other pollutants such as nitric acid, suspended nitrates, and particulates at unusually high levels of concentration. In order to eliminate such factors, it was felt to be of value to study areas with low ambient air pollution levels.

2. Design

The area chosen for the present study is the City of Upper Arlington, a middle class suburb on the periphery of Columbus, Ohio. In June, 1972, questionnaires were distributed through the elementary schools in Upper Arlington. The questionnaires were developed by the Environmental Protection Agency for the Community Health and Environmental Surveillance System (CHESS) [4] and included questions regarding demographic variables, smoking habits, and a variety of health problems. The completed questionnaires were separated into two groups; households with gas ranges; and households with electric ranges. Families that expected to move within 12 months were excluded from the sample. Among over 1,000 completed questionnaires, 17.5 percent of the households had gas ranges. In order to augment the number of gas-cooking households, additional households were visited and a second appeal was made through the schools. The final sample included 441 households, 232 of which used electricity for cooking, and 209 of which used gas. The final sample included only the families

expressing willingness to participate in the program. Table I presents the population sample whose respiratory disease experience is reported in the present paper.

TABLE I. POPULATION SAMPLE PARTICIPATING IN STUDY

	<u>Upper Arlington Study Population</u>	
	<u>Electric</u>	<u>Gas</u>
Households	232	209
Mothers	230	207
Fathers	222	197
Children, 0-12 years	407	356

Table II presents the overall age and sex distributions of the entire study sample.

TABLE II. AGE AND SEX DISTRIBUTION OF STUDY SAMPLE

Age	<u>Upper Arlington Study Population</u>	
	<u>Sex</u>	
	<u>Male</u>	<u>Female</u>
0-5	69	59
6-10	176	173
11-15	213	208
16-20	77	90
21-40	215	289
41-60	212	158
61-Up	6	7
Total	968	984

The program was initiated in November, 1972. Participants were contacted by telephone every two weeks to obtain reports on respiratory illness among members of the household during that period. A special calendar was supplied to each household for record keeping. The information obtained was recorded on two sets of records. A master card was maintained for each family in case the working mark-sense card was lost or unreadable. The master card contained all the information obtained

by the telephone interviewer. The survey continued for 26 periods to yield one full year of data.

The study population was invited to have pulmonary function screening tests for the detection of chronic respiratory impairment. Also, in order to determine the levels of NO_2 and NO , a sample of the gas and electric households were monitored for these substances.

2.1 Pulmonary Function Testing

Measures of Forced Vital Capacity and 0.75 Second Forced Expiratory Volume were made using a 10-liter dry rolling-seal spirometer. Prior to testing, each subject was instructed regarding the proper method of performing the forced vital capacity maneuver. Care was taken to insure that each subject inspired to maximum capacity and kept the back reasonably straight during forced expiration. The test was repeated a number of times until the results obtained were reproducible ($\pm 5\%$). A minimum of three trials were obtained with each subject, and the best value for each of the variables was recorded.

2.2 Monitoring for NO_x

Since the study was concerned with the possible relationship between the incidence of respiratory disease and exposure to oxides of nitrogen, it was necessary to measure this substance in a sample of the households. A total of 83 homes with gas cooking modes and 50 homes with electric cooking modes were monitored for NO_2 and NO over periods of 24 hours using the modified Jacobs-Hochheiser (J-H) method [5]. In addition, 53 outdoor samples were taken with the J-H units in the areas of the indoor monitoring. Continuous chemiluminescence measurements were also made for three-day periods in 46 homes to evaluate the instantaneous variation in indoor NO_2 and NO levels.

Peak NO_2 levels in gas cooking mode households, during cooking periods, were generally eight times higher than the 24-hour average. In several households, these peak values exceeded 100 pphm. No peak values of this type were noticed in electric cooking mode households, other than a rise in NO levels during periods of high traffic, in the homes near thoroughfares. Measurements were made in the period of January through April, 1973. Table III presents a summary of the NO_2 and NO data.

TABLE III. SUMMARY OF THE NO₂ AND NO DATA

Type	NO _x Monitoring			
	Range, pphm		Average, pphm	
	NO ₂	NO	NO ₂	NO
Gas homes	0.5-11	1-41	5	11
Electric homes	0-6	0-34	2	7
Outdoors	1.5-5	0.5-22	3	4

2.3 Statistical Method

The present study seeks to examine the relationship of a large number of variables to the incidence of respiratory illness in the study population. In this type of study, the combined effects and interactions of these variables are as important as the individual or main effects of each independent variable. Traditional analytical methods are typically bound by rather stringent assumptions concerning distributions and linearity, and frequently neglect interaction. In nearly all studies like the present one, these assumptions are known to be unwarranted, or they are incapable of being validated by examination of the data. The Automatic Interaction Detector method (AID) of Sonquist and Morgan [6], utilized in the present study, provides a multivariate approach to analysis relatively free of these restrictions. The AID program is based on a sequential analysis of variance. It selects the best set of predictive or explanatory variables with respect to the dependent variable, in this case, reported incidence of respiratory disease. It also simultaneously seeks out relationships and interactions among these variables and indicates the significance of the relationship of independent to dependent variables, in terms of the portion of the variance (differential occurrence of respiratory illness) that is explained.

AID was used for analysis of the incidence of respiratory disease in the samples of mothers and of fathers. Multiple regression was used for the analysis of the incidence in children, as will be explained in the section on Results. Table IV presents the predictive or explanatory variables used in the AID and multiple regression methods.

TABLE IV. VARIABLES USED IN THE AID AND MULTIPLE REGRESSION METHODS

<u>Mothers and Fathers - Columbus</u>		<u>Children - Columbus</u>	<u>Mothers - Long Island</u>
Explanatory Variables		Explanatory Variables	Explanatory Variables
Age (year of birth)		Age (year of birth)	Age
Group (Gas/Electric)		Group (Gas/Electric)	Group (Gas/Electric)
Cough - 3 months a year		Sex	Cough or phlegm - 3 months a year
Cough - day or night		Size of house (number of rooms)	
Cough - day or night - 3 months a year		Numbers of years family lived in community	Current cigarette smoker
Phlegm in morning		Father's educational level	Cough in morning
Phlegm 3 months a year		Chronic heart disease	Cough day or night
Phlegm day or night		Chronic lung disease	Cough day or night
Cough or phlegm 3 weeks		Chronic asthma	3 months a year
Shortness of breath		Pneumonia	Phlegm in morning
Current cigarette smoker		Croup	Phlegm day or night
Smoked 5 packs or more in life		Bronchitis	Phlegm 3 months a year
Number of cigarettes per day		Other chest infections	Shortness of breath
Age started smoking		Hospitalized	Ever smoked
Age quit smoking		Dependent Variable	Number of cigarettes per day
Number of years smoked		All respiratory illness	Exposed to irritants on job
Number of years since quit smoking			Duration of exposure to irritants
Exposed to irritant on job			Kind of irritants
Dependent Variables			Where lived as a child (up to age 20)
1. All respiratory illness (mothers and fathers)			Where lived from age 20-30
2. Lower respiratory illness (mothers)			Where lived after age 30
			Family size
			Dependent Variables
			1. All respiratory illness
			2. Lower respiratory illness

3. Results

Figure 1 presents a comparison of the annual incidence of all reported respiratory illness, per hundred persons, in the subject categories indicated. In all cases, the rates were higher in households utilizing electricity for cooking. In general, rates were highest in children under 12, and higher in mothers than in fathers. An additional comparison is presented for reported lower respiratory disease (chest colds) among the mothers. This will be related in the Discussion section to data from another study.

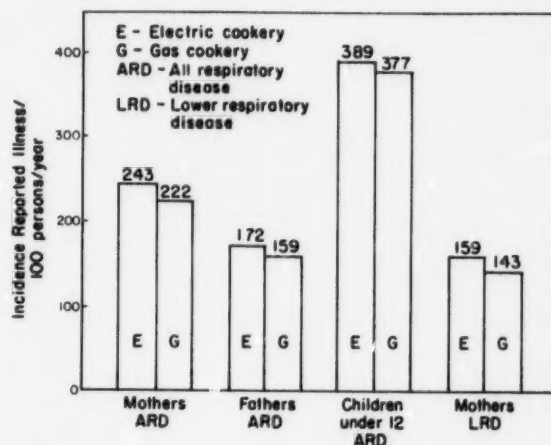
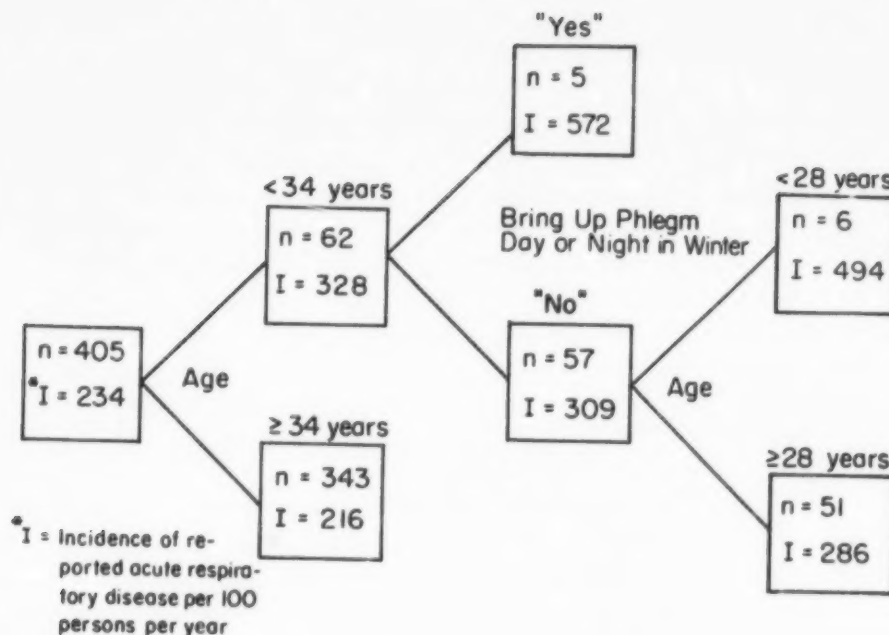


Fig. 1. Comparison of annual incidence of respiratory illness.

Figure 2 presents the AID analysis for all reported respiratory illnesses among the mothers in the Arlington sample. The overall rate for the entire population of mothers was 234 illnesses per hundred mothers per year; mothers cooking with electricity reporting an incidence of 243; while those cooking with gas reported 222. These are the figures presented in the bar graph in Figure 1. The AID analysis further indicated a higher incidence among younger mothers, who indicated in the household questionnaire that they usually bring up phlegm. Younger mothers, in general, reported higher incidence than older mothers, even when they did not initially report bringing up phlegm. Beyond this, none of the explanatory variables contributed significantly to explaining the differences in incidence. In fact, the AID analysis indicated that



2. AID analysis for respiratory illnesses among mothers - Arlington sample.

virtually none of the variance was explained whether or not the mothers cooked with gas or electricity. Figure 2 is the only AID diagram included in the present report to illustrate the method. None of the AID results proved effective in explaining differences in incidence.

AID analysis was also carried out on reports of lower respiratory illness among the mothers. The overall population of mothers had an incidence of 151 per hundred, per year. As shown in the bar graph of Figure 1, the mothers cooking with electricity had an incidence of 159 as compared with an incidence of 143 among mothers cooking with gas. However this difference was of such low significance that it could explain only 1/50 of 1 percent of the variance. In fact, in this case, all of the explanatory variables together could predict only one percent of the variance, leaving 99 percent unexplained.

AID analysis was carried out for all reported respiratory illness among the fathers. The overall incidence in the population of fathers was 160 per hundred, per year. The fathers in households with electric

cooking reported an incidence of 172, as compared with 159, in the gas household sample. However, once again the differences between the gas and the electric samples explained only 1/100 of one percent of the variance, and all of the explanatory variables together explained less than one percent. Trends were noted indicating that younger fathers reported more respiratory illness. The only other variable that may be related is smoking; those who smoked more for more years, or quit more recently, reported more illness than nonsmokers or those who quit long ago. However, it must be emphasized that none of these variables significantly explain the incidence of respiratory disease. The AID analysis does not even select the variable of gas or electric cooking for inclusion, since this has so little relation to differences in the occurrence of illness in the two groups.

The incidence of illness among children from birth to 12 years was analyzed by multiple regression. Since, in earlier analyses, all of the explanatory variables, and, in particular, the variable of gas or electric cooking contributed little to explaining incidence of illness, the expense of AID analysis was not warranted for this group, and multiple regression was deemed sufficient to answer the questions posed. The overall incidence for this population of children was 384 per hundred per year. The rate was higher among children than among the mothers or fathers. Children in the electric cooking homes had an incidence of 389 as compared with 377 in the gas cooking sample. However, once again the method indicated no predictive power.

3.1 Lung Function Tests

The entire population of the sample was invited to have lung function examinations. The tests were conducted in the manner indicated in the section on Design. Table V presents the age, sex, and group (gas or electricity) of the sample tested. Overall, approximately 42 percent of the study population was tested. Chi square (χ^2) analysis indicated no significant differences between the gas and electric household participants, in terms of age and sex representation. Table VI presents the analysis of variance of the results of Forced Vital Capacity and the 0.75 Second Forced Expiratory Volume. There were no significant differences between the groups with respect to the Total Forced Vital Capacity, and a small but significant difference appeared with regard to the 0.75 Second Forced

Volume. The participants from the gas cooking households had slightly better lung function measurements, on the average. However, the differences explained only an extremely small portion of the variance in pulmonary function, approximately one half of one percent. These tests were carried out in order to detect the possible presence of a large number of individuals with pulmonary impairment in one or the other group, since this might bias the results with regard to the reported incidence of respiratory illness. These data do not indicate such bias.

3.2 Discussion

The overall outcome of the analyses employed in the present study indicates no significant difference in reported respiratory illness between the members of households cooking with gas and those cooking with electricity. This was evident in the comparison of incidence rates among mothers, fathers, and children from birth to 12 years of age.

Additional analyses were carried out with regard to the reported lower respiratory disease among mothers in order to allow comparison of the present study results with those obtained in an epidemiologic study conducted by the Environmental Protection Agency in a suburban community in Long Island, N. Y. The latter study involved 146 households, 59 of which cooked with electricity, and 87 with gas. The study was similar to the present one in Upper Arlington, and was conducted over a period of 30 weeks. Inquiries were made regarding the incidence of respiratory illness every two weeks. Through the courtesy of the Environmental Protection Agency, computer tapes containing the data of the Long Island Study were made available to the authors so that they could be subjected to AID analysis in the same way as the Upper Arlington data. Table VII presents a comparison of the two studies with regard to all reported respiratory illness, and lower respiratory illness (chest colds) only. The data of the Long Island Study were extrapolated to a period of one year so that incidence rates could be directly compared with those of the Upper Arlington study. It is realized that this may introduce some error, since seasonal variation may be associated with changes in respiratory disease incidence. However, the basic hypothesis being tested involves comparison of incidence rates among the gas cooking and the electric cooking households in each study area. In Long Island, as in Upper Arlington, the incidence of all respiratory disease was higher among mothers cooking with electricity.

TABLE V. SUMMARY OF PARTICIPANTS IN LUNG FUNCTION TESTS

[illegible]

TABLE VI. ANALYSIS OF VARIANCE IN PULMONARY FUNCTION TESTS

Characteristics	Group 1 Electric	Group 2 Gas
Number of participants	416	405
Mean age	24.2	23.8
Mean height	61.5	61.6
Mean weight	118	116
Mean FVC	3.02 (1)	3.04 (1)
Mean FEV-75	2.32 (1)	2.39 (1)
F test for FVC (1,816 df) = 0.647		
F test for FEV-75 (1,816 df) = 4.455 (2)		

(1) Adjusted values on basis of age, sex, and height by co-variate analysis.

(2) Significant at Alpha 0.05.

In the Long Island study, the overall incidence was 302 respiratory illnesses per hundred mothers per year; those with electric cookery reporting 322, as compared with 289 in the gas cooking households. However, as in the Upper Arlington sample, these differences were insignificant. All of the explanatory variables together were only able to account for 4 percent of the variance in the Long Island Study. While this was somewhat higher than Upper Arlington, it still left 96 percent of the variance in illness unexplained.

TABLE VII. RESPIRATORY DISEASE REPORTED BY SAMPLE OF MOTHERS

		N	Rates of Illness (1)	
			All Respiratory Disease	Lower Respiratory Disease (2)
Long Island	Electric	59	322	99
	Gas	<u>87</u>	<u>289</u>	<u>133</u>
	Total	146	302	120
Upper Arlington	Electric	230	243	159
	Gas	<u>207</u>	<u>222</u>	<u>143</u>
	Total	437	234	151

(1) Reported illnesses per 100 persons per year.

(2) "Chest colds".

The Long Island sample mothers, in general, presented less lower respiratory disease (chest colds). The population incidence was 120 per hundred per year, with the mothers in the electric group reporting 99, and the mothers in the gas group reporting 133. However, again the differences were not significant, with only a minute fraction of the occurrence of illness explained. All of the predictor variables in the Long Island Study together explained only 5 percent of the incidence.

The data presented do not demonstrate sufficient differences to reject the null hypothesis, namely, no difference between the incidence of respiratory illnesses among mothers in the electric and gas cooking households. In both the Upper Arlington and the Long Island studies, insofar as the latter has been analyzed, it would appear that populations living in relatively unpolluted areas do not differ significantly with respect to reported respiratory illness in relation to mode of cookery. The underlying assumption of the present study was that exposure to NO_2 generated by gas cookery might have some effect upon the incidence of respiratory disease. If this were so, it would be reasonable to conclude that either the concentration or the length of the exposure were not sufficient to cause differences in the type of acute illness reported. It may be possible that certain other noxious agents in the general environment, as mentioned by Warner and Stevens [7], might be required to bring out the incidence described in other studies.

There may be an inherent weakness in all of the studies that have been considered due to the inability of the household respondent to convey accurate information regarding the incidence of respiratory infection in all members of the household. There may be sufficient differences between respondents to introduce error that may seriously affect the outcome of studies with relatively small samples. Certainly, it would be difficult to feel secure about the differentiation of upper and lower respiratory disease by the respondents. Such distinctions are difficult to make, and may vary greatly with the experience and perceptiveness of the respondent.

Further analysis of the specific symptoms that were reported in the present study will be presented in another paper. A second study is now in progress in which a nurse-epidemiologist will examine individuals reporting respiratory illnesses and take nasopharyngeal cultures. At the same time, examination will be made of "well" members of the same house-

hold and of members of control households in the study population. By this means, it will be possible to obtain more rigorous information regarding the meaning of a reported illness, in terms of objective physical findings and bacterial culture.

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DISCUSSION

KJELLSTRÖM (Sweden)

I understand that you only found a cause-effect relationship between smoking and respiratory disease. Why do you then spend so much time on showing prevalences among electric cooking homes and gas cooking homes? Why did you make the study and who funded it?

MITCHELL (U.S.A.)

The objective of our study was to determine if cooking with gas would increase the incidence of respiratory disease as compared to an identical population which cooked with electricity. The study was funded by the American Gas Association with cooperation from the United States Environmental Protection Agency.

GOLDSMITH (U.S.A.)

You informed us that you distributed about five thousand questionnaires and received about a thousand replies. Does this not introduce a great opportunity for bias? The bias can be aggravated by how the purpose of the study was presented to the possible respondents. Even if the purpose were disguised, how can one expect to generalize from a sample which is so poorly defined?

MITCHELL (U.S.A.)

We distributed 5,000 questionnaires to the entire elementary school population. There were several children from the same family in different grades. We received replies from a thousand families, which was more than one-half returns; this represents a fairly good sample.

RELATIONSHIP OF AIR POLLUTION TO PREVALENCE OF LOWER
RESPIRATORY ILLNESS AND LUNG FUNCTION IN
AUSTRALIAN SCHOOL CHILDREN

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ABSTRACT

The association of different levels of air pollution with prevalence of past lower respiratory illness and lung function (assessed by the maximum expiratory flow-volume curve) was studied in two populations of Australian school children - 12,000 in Sydney and nearly 300 in a steel-industry coastal city 80 miles south of Sydney (Port Kembla).

Levels of sulphur dioxide and smoke pollutants were low by international standards in Sydney, but high peak concentrations of sulphur dioxide were recorded in Port Kembla.

Children attending school in the more polluted areas of Sydney and in Port Kembla had the same prevalence of past, treated lower respiratory illness as children in the less polluted regions. A small, statistically significant correlation between lower forced vital capacity and higher pollution areas was found in older Sydney boys. This correlation was independent of the effects of other factors such as height, social class and smoking habits.

No significant decrease in maximum expiratory flow rates was found in children in the more polluted areas when the effects of their smaller vital capacities were allowed for. Interpretation of reduced expiratory flow rates attributed to pollution is difficult unless changes in vital capacity are taken into account.

1. INTRODUCTION

Chronic obstructive lung disease (chronic bronchitis and emphysema) may begin in the small peripheral airways of the lung many years before symptoms occur or conventional tests of lung function reveal abnormalities (Macklem 1972). There is epidemiological evidence that factors operating during childhood may be associated with the consequent development of chronic obstructive lung disease in adult life (Holland et al 1969, Reid 1969), and these factors may affect the small airways.

Extensive obstruction of the small airways has been found at post mortem in patients with only mild symptoms of chronic obstructive lung disease dying of unrelated causes (Hogg et al 1968). Such obstruction may remain asymptomatic for years, undetectable with conventional tests of lung function because of the low resistance of these airways to airflow, afforded by their shortness and large cross sectional area (Weibel 1960, Macklem and Mead, 1968).

Impaired lung function detected with special tests, consistent with damage to the small airways, has been found in asymptomatic smokers who have normal spirometry (Ingram and O'Cain 1971); following 'upper' respiratory infection (Picken et al 1972); and after exposure to high levels of air pollutants including ozone especially when the subject exercises as well (Bates et al 1972). While the antecedent relationship of disease in the small airways to chronic obstructive lung disease remains to be established, assessment of the effects of such factors as air pollution on the function of the peripheral airways in populations is justified (Bates 1972). Such assessments are not easy in epidemiological

studies because of the lack of a totally satisfactory field test for this purpose (Macklem 1972).

The present study of Australian school children commenced in 1971 and is designed to assess the effect of various factors on the development of normal lung function between the ages of 7 and 17 years. Factors including acute respiratory illness, poor social environment, cigarette smoking and air pollution are being studied. Children are examined annually. Ventilatory function is measured from the maximum expiratory flow volume curve.

This paper outlines the methods used in the study of the relationship of low concentrations of air pollution with sulphur dioxide and smoke with the ventilatory function and prevalence of respiratory illness of Australian children, and some early results.

2. METHODS

2.1 Sampling

Two samples of children were drawn, the larger one from Sydney, and the smaller from Port Kembla. The base population from which the larger sample was drawn was of children attending all school within 20 miles of central Sydney, in third grade of primary school (7-8 years) or first form of secondary school (12-13 years) in 1971. The sample contained approximately 1 in 6 third grade pupils and 1 in 7 first formers of the base population. Almost 93% of the sample (12,000) were studied, the remaining children either being absent or lacking parental consent. Slightly more children not examined were of parents of low social class and of non-Australian birthplace than were children in the study.

To observe the effects of occasional high levels of pollution (in comparison with the effects of relatively constant low levels in Sydney), 283 children in third to sixth grade (aged 7-13 years) were studied in Port Kembla. Port Kembla is a coastal steel-works town 60 miles south of Sydney. Ninety percent of the school population were examined with a similar non-participant bias as in Sydney.

2.2 Measurement of Lung Function

The maximum expiratory flow volume (MEFV) curve was derived by computer analysis of the largest of two or three forced vital capacity manoeuvres which were recorded for each child on magnetic tape using portable equipment taken to the school (Leeder et al 1974). The MEFV curve was chosen because it provided maximum expiratory flow rates during the latter half of forced maximal expiration as well as conventional spirometric values. These later flow rates are considered less effort-dependent and more reflective of resistance within the smaller airways than are earlier (e.g. peak) flow rates (Macklem and Mead 1968).

From the MEFV curve were obtained values for peak expiratory flow rate (PEFR), forced vital capacity (FVC), timed expiratory volumes ($FEV_{0.5 \text{ sec}}$, $FEV_{0.75 \text{ sec}}$) and the maximum expiratory flow rates ($\dot{V}_{\text{max}}$) at 50, 25 and 10% FVC (Figure 1). Measurements were converted to body temperature equivalents.

2.3 Collection of Demographic, Social and Medical Data

Demographic details were obtained by written questionnaire from the children's parents as were parental occupations and

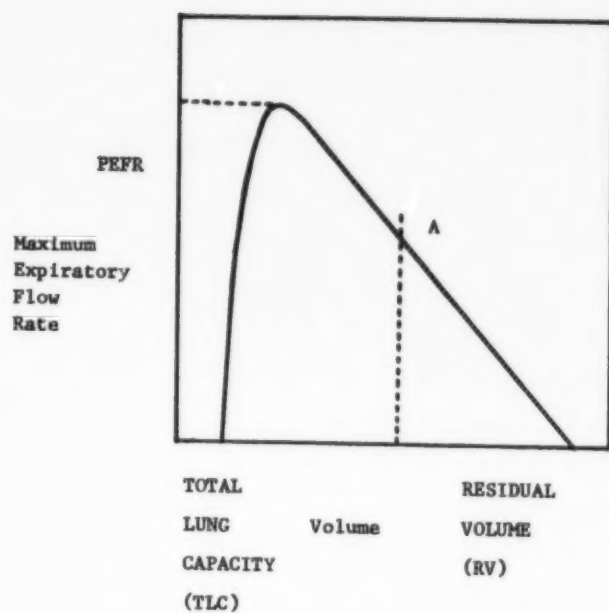


Figure 1 Schematic maximum expiratory flow volume curve, from which may be obtained forced vital capacity (TLC-RV) and peak expiratory flow rate (PEFR) as well as maximum expiratory flow rates at any point during the FVC manoeuvre.

The interval A-RV commencing at 50% FVC is less effort dependent and more sensitive to minimal airways damage than the flow rates along the curve from TLC to A.

countries of birth. Details of past respiratory illness were sought using the same questionnaire, and information about the smoking habits of children was obtained by confidential interview (Leeder and Woolcock 1973).

2.4 Air Pollution Measurements

Annual average concentrations of sulphur dioxide (SO_2) and smoke density were obtained for selected regions of Sydney and Port Kembla (as well as peak hourly concentrations for the latter) from the statutory pollution control body in New South Wales (Pollution Report 1972). Schools were then ranked by our own estimates, based upon this information, according to their probable pollution exposure.

2.5 Analysis

Analyses of variance in the measurements of lung function of 1942 boys aged 12-13 years in 1971 (non-smokers) were computed using a regression technique. To exclude the confounding effects of social class, height, weight and age, these several factors were included as covariates in all analyses. Similarly, to remove the effects of forced vital capacity upon measurements of expiratory flow rate (as they were strongly correlated), it was included as an additional covariate in these analyses.

The regressions with height and mean values of lung function measurements of children living in Port Kembla were compared with those of children living in Sydney.

The frequency of a history of past respiratory illness was compared for boys and girls of all ages living in the more and

less polluted areas of Sydney, and for children living in Port Kembla with those of Sydney children, and examined for significant differences using the χ^2 test.

3. RESULTS

3.1 Air Pollution Levels

The annual average concentrations of sulphur dioxide varied from approximately 120 to 40 micrograms/cubic metre (m^3) in the most to least polluted areas of Sydney in 1971. Concentrations of this pollutant has been declining slowly for several years in Sydney (Pollution Report 1972) but the geographical distribution has not changed substantially.

The annual average SO_2 concentration recorded in Port Kembla in 1972 was 95 micrograms/ m^3 with the highest 24 hour average of over 1000 micrograms/ m^3 and the highest hourly reading in excess of 3000 micrograms/ m^3 .

Smoke density varied in Sydney from 22 to 60 micrograms/ m^3 and was distributed in a similar geographical pattern to the SO_2 . Dust deposit in Port Kembla ranged from 10 to 30 grams/ m^2 / month and smoke, measured as coefficient of haze (COH), had an annual average of 1.2 COH units/1000 linear feet.

3.2 Prevalence of Respiratory Illness

The prevalence of a history of past, treated respiratory illness in boys and girls in Sydney is given in Table 1. Although the prevalence rates varied considerably from school to school, this was not dependent on pollution rating. Similar prevalence

rates were obtained in Port Kembla to those in Sydney children of the same age.

TABLE I

Percentage prevalence of past treated bronchitis, asthma, and other chest or lung problems in a sample of Sydney (Australia) school children in 1971.

7-8 years old n = 1,246			12-13 years old n = 2,517	
Disease	<u>Boys</u>	<u>Girls</u>	<u>Boys</u>	<u>Girls</u>
Asthma alone	2.2	1.0	2.1	1.2
Bronchitis alone	24.0	22.0	20.5	16.2
Asthma with bronchitis	7.2	4.4	5.9	4.3
Other chest or lung problems alone or with asthma and bronchitis	6.1	5.5	7.2	6.2

3.3 Lung Function Measurements

In Sydney boys aged 12-13 years in 1971, significant variance ($F = 15.9$) in forced vital capacity was attributable to the pollution factor with a significantly lower mean FVC (4.8%, $p < .001$)

among those boys attending schools in more polluted areas (Table 2). Results are not yet available for older girls and the younger children in our study.

TABLE II

Analysis of variance in lung function measurements attributable to an air pollution factor in 1924 boys aged 12-23 years in Sydney in 1971.

MEASUREMENT	MEAN SUM OF SQUARES		F
	Source (Pollution)	Error	
Peak expiratory flow rate	2.279	0.929	2.45
† FVC	9.190	0.577	15.93***
†† FEV _{0.5}	0.243	0.098	2.48
†† $\dot{V}_{\max}$ 50% FVC	4.399	0.723	6.08**

*** $p < .001$

** $p < .01$

† Height, weight, age and social class as covariates
 †† As for †, with FVC as additional covariate.

A small amount of variance in $\dot{V}_{\max}$ 50% FVC was still attributable to the pollution rating even after the inclusion of FVC as a covariate in the analysis but the reduction of mean value was not significant (2.1%, $p > .05$). While other measurements of lung function were negatively correlated to a small degree with pollution rating, the mean differences were all small and entirely accounted for by the reduction in mean vital capacity.

Regression coefficients and mean values for prediction of forced vital capacity and $\dot{V}_{\max}$ 50% FVC according to height in the

Port Kembla children did not differ significantly from those found in Sydney children.

4. DISCUSSION

Sydney enjoys clean air by international standards. A spreading suburbia affords the opportunity to study the effects of relatively small gradients of pollution without the interference of marked social stratification or urban rural gradient. Photochemical pollution has increased in recent years and more information on its magnitude is now becoming available and will be considered in future studies.

In marked contrast to past treated lower respiratory illness, particularly asthma, the pollution factor in our study was not related to any large reductions in $\dot{V}_{\max}$, particularly during the latter half of forced expiration. That no variation in the prevalence of respiratory illness could be attributed to pollution is consistent with this observation.

Several explanations may be offered for our findings. Firstly, the concentrations of pollution we have been studying may be entirely safe, and cause no trouble to the lungs of children. The small reduction in FVC would then have to be attributed to some other factor not included in our analyses of covariance, or some non-linear effect of one of the factors already included in the analysis.

Secondly, the measurements of air pollution, lung function and respiratory illness may all be too insensitive to detect subtle changes. However the geographical stability of the pollution patterns, and the known association in our study of impaired lung

function with positive answers to our questions about past respiratory illness make these explanations unlikely. It may however be profitable to investigate the association of certain respiratory symptoms both with specific impairments lung function and pollution gradients in the future in determining the dose-response relationship between impaired respiratory health and pollution levels.

Thirdly, the lower FVC observed in older boys in the more polluted areas of Sydney may simply reflect a variation in their lung size, perhaps due to altered growth characteristics of the lung and airways when exposed to low levels of pollution over a long time. Lung volume measurements would be required to determine if this were the case.

Changes in lung function attributable to low levels of pollution may be different from those due to high concentrations. Other studies have revealed a greater frequency of respiratory illness and reduced peak expiratory flow rates in children exposed to high concentrations of pollution (Holland et al 1969, Toyama 1964) sometimes in the presence of a normal FVC. Low concentrations of pollution may alter the growth pattern of the lung, whereas higher levels alter the function of the large airways and hence reduce the PEFR (Bates 1972). Zapletal et al (1973) found some evidence of impaired airway function, using the MEFV curve, in 6 of 111 children, 10 to 11 years old who lived in Most, Czechoslovakia, but the pollution levels there were substantially higher than in our study.

The Port Kembla study was of a small number of children, and small differences in lung function may not be apparent for this

reason. However, it was clear that no marked long-term effects on lung function could be attributed to occasional very high concentration peaks.

5. CONCLUSIONS

Thus far, the study of the association of air pollution by low levels of sulphur dioxide and smoke with the prevalence of lower respiratory illness and lung function in Sydney children has not revealed any long term effects apart from a marginally lower forced vital capacity in older boys. The study points up the need to allow for changes in lung growth characteristics in children living in different areas before concluding that isolated measurements of reduced expiratory flow rates represent lung or airway damage.

Acknowledgements:

We thank Dr. A. Bell of the division of Health and Pollution Control of the Health Commission of NSW for providing measurements of pollution, and the staff and children of the survey schools for their participation. The study was supported by the Australian Tobacco Research Foundation and S.R. Leeder was in receipt of an Australian National Health and Medical Research Council Scholarship.

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DISCUSSION

JOOSTING (Netherlands)

A small, statistically significant correlation between lower forced vital capacity and higher pollution areas was found in older Sydney boys. You mentioned that this correlation was independent of the effects of other factors such as height, weight and social class. You did not mention the influence of smoking explicitly. Could smoking habit be a relevant explanatory variable if we recognize the fact that nowadays smoking starts already at the age of ten?

LEEDER (Australia)

Regular cigarette smoking is certainly an important factor to consider when measuring ventilatory capacity, even in children as you suggest. We included a variable which reflected the age of onset of smoking and the amount smoked in our calculation of effects of factors affecting lung function, but the factor was of no significance in explaining reduced values. This may well be due to the relatively young sample we have studied, and we will continue to investigate the effect of smoking in our ongoing studies.

RESPIRATORY SYMPTOMS AND VENTILATORY CAPACITY
IN A COHORT OF LONDONERS BORN IN 1952-3

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ABSTRACT

In the first stage of this study 800 Londoners who reached age 18 in 1970, and who were exposed in the neo-natal period to very high concentrations of pollutants during the London fog of December 1952 were examined, using a modified form of the MRC Questionnaire on Respiratory Symptoms. Ventilatory capacity was also measured, using a portable spirometer and a peak flow meter. In the second stage, a further 800 subjects who reached age 18 in 1971, and were not exposed to the 1952 episode, were examined in the same way.

Results from these two samples have now been compared, and no differences have been found in the prevalence of respiratory symptoms, nor in the mean values of FEV₁, FVC and PEF, between subjects born before the fog and those born after it.

Respiratory symptoms were much commoner among the smokers than among the non-smokers and there were small differences in ventilatory capacity between these categories. The main factor associated with lowered ventilatory capacity was a history of respiratory illness, and in view of earlier findings, this may indicate an indirect long-term effect of exposure to pollu-

1. Introduction

In an earlier study, Douglas and Waller [1] found a relationship between the incidence of lower respiratory tract infections in children and exposure to air pollution, as estimated from domestic coal consumption in the areas where they lived. This relationship was already evident when the children were nine months old, and it persisted at least until age 15. Several other studies in the United Kingdom have shown a higher incidence of respiratory diseases or reduced ventilatory capacity among children living in relatively polluted areas (Lunn *et al.* [2], [3], Holland *et al.* [4], Colley and Reid [5]) and the possibility that this has some bearing on the gradual development of chronic bronchitis has been discussed by these and other authors. In each of the above-mentioned studies exposures to pollution were assessed in terms of mean values over long periods, and there was no way of determining whether occasional exposures to very high concentrations were of special importance. The most outstanding episode of high pollution on record, in terms of adverse effects on health, was the London fog of December, 1952. It was estimated (Ministry of Health [6]) that some 4,000 people died prematurely as a result of exposure to the very high concentrations of smoke, sulphur dioxide and associated pollutants that persisted then for four days. These "excess" deaths were mainly among the elderly, but a small proportion were of infants less than one year old. There was evidence of an increased incidence of acute respiratory disease at the time, but there was little quantitative information on its impact on infants in particular.

The opportunity has now been taken to study respiratory symptoms and ventilatory capacity among two samples of Londoners, one born during 1952, before the fog, and the

other during 1953, just after it.

2. Method

Three small areas of Greater London, chosen to contain about 1% of the total population and a cross-section of all social classes, were selected, and within these the names of all residents reaching age 18 during 1970 were listed from the electoral registers. After sending out introductory letters, each subject was visited in his (or her) own home in the evenings, phasing the interviews over a 12 month period from October 1970. The same procedure was adopted for the second sample, except that 1971 registers were used and the interviews started in October 1971. The average age at interview was then just the same in the two samples, and although there may have been some biases in the registers themselves, the two samples were very well matched in respect of every factor other than the designed one-year difference in date of birth.

The aim in this study was to compare the results for pre-fog and post-fog births, using the day on which the fog finally cleared - 9th December, 1952 - as the dividing line, and restricting these contrasts to London-born subjects. Local contrasts between the three areas were not sought, since it was known that there had been much movement of families within London since 1952.

A modified MRC Questionnaire on Respiratory Symptoms (Medical Research Council [7]) was used. All the standard questions were included, with additional ones on childhood diseases, place of birth and home conditions when the subjects were babies. (Most of the subjects were still living with their parents, who helped with this latter information when necessary.) Five spirometric measurements were made on a portable instrument (McDermott *et al* [8]),

recording FEV₁ and FVC each time, followed by five measurements of peak expiratory flow (Wright and McKerrow [9]). Calibration checks were made throughout the field-work and all instruments were returned to the laboratory at regular intervals to maintain comparability.

3. Results

The total number of subjects seen in the two years was 1586, representing 88% of the available sample (people who had already left the district permanently were discounted but students who were away only in term-time were included). The proportion of males (52.5%) was a little higher than that of females, and 86% of the total were born in Greater London.

Over 40 questions on respiratory symptoms, previous illnesses, smoking habits and environmental conditions were asked of each subject, and the results were analysed initially in terms of the proportion of positive answers to individual questions. Not all the subjects who reported persistent phlegm also said that they had a persistent cough, and despite efforts to ensure that the answer related to phlegm from the chest, there appeared to be some confusion with phlegm from the nose in this young age-group (nasal catarrh was the most commonly reported symptom, with nearly 40% reporting catarrh in the winter). The proportion giving positive answers to both the cough and phlegm questions (Q5 and Q10) was therefore determined as an index of productive cough, indicative of simple chronic bronchitis (Medical Research Council [10]). One other general feature was that the proportion of girls reporting slight breathlessness (shortness of breath when hurrying on level ground or walking up a slight hill) was more than twice that of the boys. This marked difference

was found in all areas throughout the survey, and it may be characteristic of adolescent girls, but this mild degree of breathlessness was not in general related to reduced ventilatory capacity.

Results from only the principal questions are shown in the tables below. The wheezing question included (Q16) is that relating to attacks of shortness of breath with wheezing, but normal between attacks (indicative of asthma), and any chest illness that had interrupted usual activities for more than a week during the past three years is included under Q21. The group of questions Q22 to 31 relates to previous illnesses, mainly bronchitis, asthma and pneumonia, and the proportion of subjects reporting one or more of these is quoted. This information depends on recall (usually by the parents) over an 18 year period, and it is therefore not very reliable.

Preliminary analyses were done on the ventilatory capacity measurements to determine the relationship with height and weight. As in other studies a linear relationship with height was found, and the results quoted in the tables have been standardized to heights of 174 cm for men and 162 cm for women. After standardizing for height there was no consistent variation with weight, and since all subjects were virtually the same age (the mean age at interview was 18.7 yr) there was no need to standardize for age. Results in this paper are based on the highest of the five measurements of FEV_1 , FVC and PEF made on each subject, but the mean of the last three has also been used.

TABLE I

PREVALENCE OF RESPIRATORY SYMPTOMS (% POSITIVE) AND VENTILATORY CAPACITY AMONG SUBJECTS BORN BEFORE AND AFTER THE 1952 FOG. LONDON-BORN SUBJECTS ONLY.

Question	Males		Females	
	Pre-fog	Post-fog	Pre-fog	Post-fog
Persistent cough	8.9	7.9	8.7	5.9
Persistent phlegm	10.3	8.4	6.0	6.2
Cough and phlegm	4.5	4.7	2.7	2.9
Breathlessness (Gr.2+)	11.7	13.1	26.8	27.1
Attacks wheezing	12.7*	7.2	4.7	7.1
Chest illnesses	12.7	10.0	12.8	14.5
Previous illnesses	30.2	24.3	23.2	24.5
FEV ₁ litres, mean	4.34	4.39	3.20	3.26
FVC litres, mean	5.16	5.12	3.71	3.76
PEF l/min, mean	549	546	431	425
No of subjects	291	428	298	339

* Significant difference ($P < 0.05$, χ^2 test)

Comparisons between pre-fog and post-fog groups are shown in Table I. For most of the symptoms and measurements considered there were no significant differences between the results for subjects born before the fog and those born

after it. Among males the proportion reporting attacks of shortness of breath with wheezing (Q16) was higher for the pre-fog than for the post-fog subjects, but this was not consistent between the two sexes.

T A B L E II

PREVALENCE OF RESPIRATORY SYMPTOMS (% POSITIVE) AND VENTILATORY CAPACITY AMONG NON-SMOKERS AND SMOKERS

Question	Males		Females	
	Non-smokers	Smokers	Non-smokers	Smokers
Persistent cough	6.2*	12.9	4.2*	12.5
Persistent phlegm	7.3*	12.4	2.6*	12.5
Cough and phlegm	3.8	6.6	0.6*	7.5
Breathlessness	7.9*	16.3	18.7*	45.1
Attacks wheezing	9.1	9.7	5.4	7.5
Chest illnesses	10.2	12.9	8.7*	21.6
Previous illnesses	25.8	28.4	22.7	27.6
FEV ₁ litres, mean	4.42*	4.32	3.26*	3.18
FVC litres, mean	5.15	5.12	3.74	3.74
PEF l/min, mean	550	545	432*	422
No of subjects	453	380	497	255

* Significant difference ($P < 0.05$, χ^2 test for questions and t test for ventilatory capacity)

The main factor affecting the prevalence of symptoms was smoking, even though smoking histories in these young subjects were short, and Table II shows results for smokers compared with those for non-smokers (the latter group includes ex-smokers). The prevalence of the main respiratory symptoms (cough, phlegm and breathlessness) was

T A B L E I I I

PREVALENCE OF RESPIRATORY SYMPTOMS (% POSITIVE) AND
VENTILATORY CAPACITY IN RELATION TO HISTORY OF RESPIRATORY
ILLNESSES

Question	Males		Females	
	Pneu- monia	No ill- nesses	Pneu- monia	No ill- nesses
Persistent cough	11.8	7.7	15.1	5.8
Persistent phlegm	10.3	7.9	5.7	5.1
Cough and phlegm	7.4	3.6	5.7	2.3
Breathlessness	14.7	9.5	37.7*	23.0
Attacks wheezing	13.2*	3.0	11.3	3.2
Chest illnesses	23.5*	5.4	24.5*	7.7
FEV ₁ litres, mean	4.21*	4.42	3.17	3.25
FVC litres, mean	5.05	5.14	3.74	3.74
PEF l/min, mean	525*	553	417	430
No. of subjects	68	608	53	570

* Significant difference ($P < 0.05$, χ^2 test for questions and t test for ventilatory capacity)

significantly higher among smokers than among the others, and the contrast was particularly marked for females. There were no differences in FVC between the groups, but the mean values of FEV_1 were a little lower among smokers than among the others (in females there was a significant difference in PEF also). There was no reason to believe that differences in smoking habits could have biased the results in Table I, and further analyses showed that the findings were still the same when smokers and non-smokers were considered separately.

Subjects who said that they had suffered from bronchitis or asthma during their childhood were seen to have a high prevalence of current respiratory symptoms and reduced ventilatory capacity. Those who reported at least one illness with pneumonia (or pleurisy) also tended to have a higher prevalence of symptoms and lower ventilatory capacity than others (Table III). There was also a relationship between current respiratory symptoms and ventilatory capacity, the greatest contrast being between subjects reporting persistent cough with phlegm and those free from respiratory symptoms.

The results were considered in relation to many other factors that had been studied, including the social class of the family, the size of family, the type of house in which they lived and the season of birth, but none of these had any substantial or consistent effect on the prevalence of symptoms, nor on ventilatory capacity. Questions on parental smoking had been asked, and there was some evidence that this was related to an increased prevalence of symptoms, but in view of the general correlation between the subjects' own smoking habits and those of the parents, it was difficult to determine whether this was an independent effect.

4. Discussion

The results of this study have shown quite clearly that exposure in infancy to the London fog of December 1952 has had no dominant effect on the development of respiratory symptoms up to age 18. The maximum age of subjects in this study at the time of the fog was 9 months, and it is possible that such young children may have been kept indoors, slightly (but by no means wholly) protected from the pollution. A more extensive study would be required to follow up people who were a little older at the time of the fog. The most important point may however be that each of the two groups studied (pre-fog and post-fog) was exposed in the remaining childhood years to the high levels of pollution that prevailed in London through the 1950's and into the 1960's. Although the 1952 fog has not been matched in severity, there have been many episodes of high pollution in London, for example in January 1956, December 1957 and December 1962 (Waller and Commins [11]). There are few data for comparable groups of 18-year-olds brought up in relatively clean conditions, but the prevalence of respiratory symptoms in the whole of the sample was higher than in a group of medical students studied at the same age (Lawther, Brooks and Waller [12]). This latter group must however be regarded as selected, and further work is planned on general population samples in London and in a relatively "clean" area.

The importance of respiratory illnesses in childhood in relation to the subsequent development of respiratory symptoms, which was apparent in this study, has also been seen in some other investigations. In the longitudinal study of a sample of children born in 1946, the prevalence of symptoms at age 20, although affected mainly by smoking, has been found to be related to the past history of

respiratory illnesses (Colley, Douglas and Reid [13]). It had already been shown (Douglas and Waller [1]) that the incidence of lower respiratory tract infections in this same sample was related to the estimated exposure to pollution and there may therefore be a link between childhood exposures to pollution, repeated respiratory infections and the subsequent development of chronic bronchitis. The retrospective information on childhood illnesses in the present study of 1952-53 born subjects was not adequate to substantiate this point any further, but the dramatic changes in pollution in London during the last 20 years may provide an opportunity for further studies, in which the prevalence of symptoms in the present 1952-53 cohort can eventually be compared with that in a 1962-63 cohort, born around the time of the last of the major London fogs, and finally with that in a 1972-73 cohort, born into the "clean air" conditions of today.

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DISCUSSION

JACOBSEN (U.K.)

The author suggested that the observed higher prevalence of respiratory symptoms among those who reported respiratory disease in early life may indicate that exposure to the 1952 fog may have had an indirect effect (via early childhood disease). Is this not a hypothesis that can be verified from the data? Would it not imply that children exposed to the smog should have shown higher symptom-prevalence?

WALLER (U.K.)

It is true that if exposure to the 1952 fog had had an indirect effect on the subsequent development of respiratory symptoms, by enhancing the incidence of respiratory illnesses among babies at the time, then this should have shown up in the contrasts between the pre- and post-fog samples. The problem is that we do not have an adequate index of the exposure of individual members of the samples to pollution at that time. Whether they were kept indoors or taken outside during the fog would have made a material difference to their exposure to at least some components of the pollution and it would have been interesting to have been in a position to compare results in relation to an index of exposure within the pre-fog sample.

STUPFEL (France)

You show that there are differences between males and females concerning phlegm but not concerning FEV. We have been able to demonstrate experimental sex related differences in acute mortality between males and females in mice and rats exposed to high concentrations of carbon monoxide and automotive exhaust gas. Do you have data for mortality differences related to sex and to acute air pollution episodes independent of smoking habits and occupational exposure?

WALLER (U.K.)

There are sex-related differences in the prevalence of some of the symptoms considered in our study and in the absolute values of the ventilatory capacity measurements, but in general factors such as smoking have the same kind of effect on these quantities within each sex.

We do not have detailed information on mortality in the 1952 fog by sex, but full details of day-to-day changes in mortality by age, sex and cause have been collected for more recent periods and these will be reported soon.

KEVANY (Ireland)

Would age at first school attendance have been a more sensitive time to judge pre- and post-smog effects as school going children would be subject to more uniform exposure through travelling to school.

WALLER (U.K.)

Ages under 1 year were chosen for the present study because of evidence from other work that babies in that age range appeared to be particularly susceptible to environmental influences. The age-range 5 - 6 could provide an alternative: the children may then be affected more by cross-infections on first starting school but at least it is known that they have to go out in all weathers. We have some information on children who were aged 6 in 1952, from our earlier study of the "1964 cohort" and this will be examined further.

A STUDY ON HEALTH EFFECT INDICES CONCERNING POPULATION IN CADMIUM-POLLUTED AREA

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ABSTRACT

1. *Stages of Cd metabolism, classified by urinary Cd excretion and tubular function.*

Accumulation stage: the stage when no abnormal increase of urinary Cd excretion is found, (school age in low and high polluted area).

Saturation stage: the stage when increase of urinary excretion of low molecular weight protein is not clear, and there is found an increase of urinary Cd excretion, (adult age in low polluted area).

Excretion stage (the former term): the stage when a sharp increase of urinary excretion of Cd, Cu and low molecular weight protein is observed, (adult age in high polluted area).

Excretion stage (the latter term): the stage when excretion of low molecular protein in urine is still clear, but excretion of Cd in urine has tendency to decrease, (adult age in high polluted area).

2. *Indices of tubular disorder by Cd intake.*

Lysozyme, B₂-M G and Proline in urine are reasonable indices

for tubular dysfunction. The pattern of proline excretion in urine is different between male and female.

Increase of B_2 -M G in serum is reasonable index of tubular dysfunction, though it is often seen in aged persons having no finding of tubular dysfunction.

It seems that female has other accelerating factor concerning development of tubular dysfunction by Cd intake. Tubular disorder by intake of Cd polluted rise is accelerated by aging.

It seems that Cd level in urine is reflected to Cd level in blood and, on the other hand, Cu level in urine is not related to that in blood.

The meaning of Cu intake for the cause of tubular dysfunction is not possible to be ignored.

Introduction

Cadmium (Cd, in abbreviation) pollution of rice was noticed in the areas around Ikuno Mine (located in the central part of Hyogo Prefecture) in the early spring of 1971. Then, Cd pollution health effect surveys were made on inhabitants of 30 years or more (the number, 13,052), in the areas, where rice contained Cd of over 0.4 ppm, and also in the areas adjacent to them. The total number of those areas are 9, which are subdivided into 54 districts.

Based on the results of the surveys, the following considerations were made on Cd health effect indices.

All subjects belonged to farmers' family and, as a staple food, ate rice produced in the areas where they lived.

High-polluted area; an area where 0.6-1.0 ppm of Cd was detected in unpolished rice. (Copper (Cu, in abbreviation) concentration in the same rice was about 6 ppm.) (H in abbreviation)

Low-polluted area; an area where around 0.3 ppm of Cd was detected in unpolished rice. (Cu in the same rice was about 3 ppm) (L in abbreviation)

Non-polluted area; an area where no Cd environmental pollution was found and Cd below 0.1 ppm was detected in unpolished rice. (Cu in the same rice was about 2 ppm) (N in abbreviation)

Time of survey;

NO.1. April, 1971. At that time, the subjects were recommended not to eat rice containing Cd over 1.0 ppm.

NO.2. October, 1971. 6 months after the recommendation.

NO.3. June, 1972. About 1 year after the recommendation.

NO.4. June-October, 1973. About 2 years after the recommendation.

Results

I. Relationship between intake of Cd-polluted rice and urinary excretion.

1. Mean Cd concentrations in urine and hair of adults and schoolchildren, by Cd concentration in unpolished rice harvested in the areas where they lived. (Time NO. 1)(Table 1)

(1) Mean Cd concentration in urine of adults in H area is higher than that of L area. (2) Cd concentration in urine of schoolchildren is not related to Cd pollution. (3) Cd concentration in urine of adults is higher than that of schoolchildren. (4) Cd concentration in hair of adults is higher than that of schoolchildren. (5) Cd concentration in hair is not

Table 1. Mean Cd concentrations in urine and hair of adults and school-children, by Cd concentrations in unpolished rice harvested in the areas where they lived.

(Examined in April, 1971.)

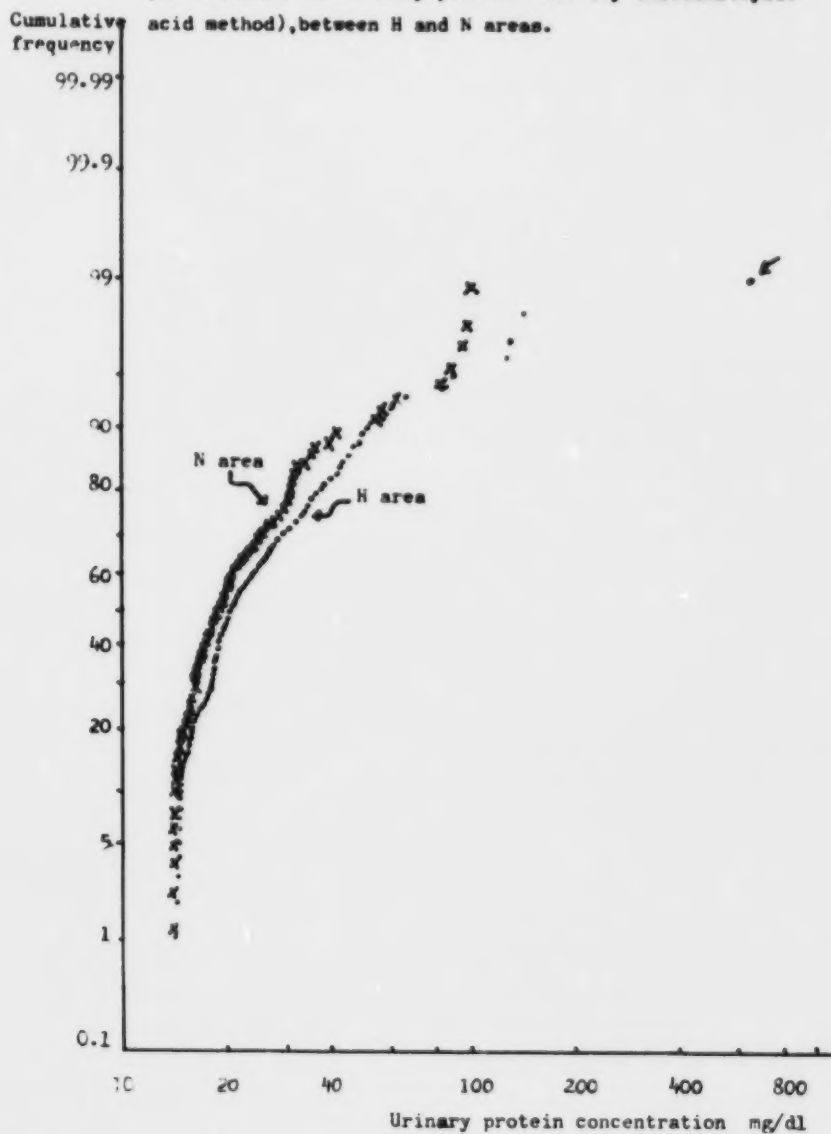
Cd concentration in unpolished rice	Number of area	Adult			School-children	
		Urinary protein positive rate	Cd in urine	Cd in hair	Cd in urine	Cd in hair
ppm		%	μg/l	μg/g	μg/l	μg/g
0.33	14	13.4	7.1	0.67	2.3	0.49
0.35	11	10.2	7.7	0.82	1.8	0.41
0.61	3	6.9	11.1	0.78	3.4	0.37
0.88	5	12.1	13.0	0.73	3.5	0.67
1.10	6	13.5	14.2	1.06	2.0	0.63

Table 2. G/A ratio and concentration of protein, Cd and Cu in urine by Cd pollution. (Protein positive persons)

Cd concentration in unpolished rice	n	G/A ratio	protein in urine	Cd in urine	Cu in urine
0.33 ppm	35	0.60	11.2 mg/dl	5.8 μg/l	34.7 μg/l
0.35	34	0.62	7.4	5.5	36.6
0.61	49	1.47	4.9	7.8	44.7
0.88	50	1.53	5.1	11.7	50.1
1.10	55	1.80	4.7	10.5	49.0

The method of the quantitative analysis of urinary protein is Kings-bury-Clark's.

Fig. 1 Comparison of cumulative frequency distributions of logarithmic values of urinary protein concentration (by biuret method), about those subjects who showed positiveness for urinary protein test (by sulfosalicylic acid method), between H and N areas.



2. G/A ratio and geometrical mean of concentrations of protein, Cd and Cu in urine of subjects who showed positive for urinary protein test (by TCA method), by Cd concentrations in unpolished rice harvested in the areas where they lived. (Time NO.1) (Table 2)

(1) G/A ratio and Cd or Cu concentrations in urine in H area are higher than those of L area. (2) Concentrations of protein in urine is not related to Cd pollution.

3. Prevalence of glucosuria.

(1) prevalence of glucosuria is higher in H area than in L area. (By age and sex matched data) H area: 4.1 %, L area: 2.7 % (combistix test paper) (Time NO.2)

4. Comparison of cumulative frequency distributions of logarithmic values of urinary protein concentrations between H and N area. (Time NO.3) (Fig.1)

(1) Subjects in non-polluted area were 82, who were the whole number having showed urinary protein concentration of 14 mg/dl or more.

Subjects in H area were 99, who were sampled, matched with them in N area concerning compositions of age and sex, and also showed urinary protein concentration of 14 mg/dl or more.

This means this comparison is the complete comparative study on such subjects who showed relatively high urinary protein excretion, between H and N areas. Both distribution diagrams are quite similar except one (marked with an arrow) in H area. Therefore, the existence of some heterogeneous group, i.e., a group of high urinary protein excretion, seems to be very unlikely.

5. Comparison of urinary protein concentrations between H and N areas by biuret method with sex and age matched data. (Time NO.3)

(1) Geometrical mean of H area : 2.19 mg/dl (n=376), L area : 2.42 mg/dl (n=250). It was not shown the significant difference between H and L areas.

6. Relation between Cd and protein or between protein and G/A ratio in urine. (Time NO. 2)

(1) Relation between Cd and protein in urine, by Cd concentrations of unpolished rice was not significant. (2) Relation between G/A ratio and urinary protein concentration was significant in H area.

II. Relationship among aging, Cd intake and urinary Cd excretion, protein or others. (Time NO.2)

1. Relation between aging and urinary Cd concentration was unclear. (Table 3)

Table 3. Relation among G/A ratio, Cd and Cu in urine by aging.
(Protein positive persons)

	Age	n	Low- Polluted area	n	Highly- Polluted area
G/A ratio	30~39	8	0.47 ± 0.17	16	0.93 ± 0.17
	40~49	11	0.62 ± 0.46	19	1.24 ± 0.88
	50~59	8	0.55 ± 0.26	23	1.56 ± 1.07
	60~69	18	0.70 ± 0.48	47	1.75 ± 0.72
	70~79	17	0.90 ± 0.60	62	2.21 ± 0.67
	80~89	6	1.43 ± 0.47	13	2.02 ± 0.74
Cd concentration in urine. ($\mu\text{g/l}$)	30~39	8	7.75 ± 5.00	16	11.50 ± 9.64
	40~49	11	8.45 ± 5.14	19	13.10 ± 7.70
	50~59	8	6.00 ± 4.27	23	14.04 ± 9.49
	60~69	18	6.22 ± 3.88	47	12.44 ± 5.92
	70~79	17	10.29 ± 6.70	62	11.61 ± 6.58
	80~89	6	8.33 ± 3.93	13	11.51 ± 6.29
Cu concentration in urine. ($\mu\text{g/l}$)	30~39	8	53.8 ± 37.6	18	43.3 ± 26.0
	40~49	9	39.4 ± 16.7	21	44.0 ± 21.0
	50~59	8	32.5 ± 27.1	22	56.8 ± 37.1
	60~69	18	33.9 ± 19.1	46	53.7 ± 27.8
	70~79	17	53.2 ± 29.2	61	62.1 ± 30.4
	80~89	4	47.5 ± 20.6	12	105.8 ± 77.7

2. Increase of urinary Cu concentration or G/A ratio was related to age. (Table 3) Urinary protein and glucose were related to age too. And these increases were more accelerated in H area than in L or N area.

III. Relationship between G/A ratio and Cd or Cu concentration in urine or hair. (Time NO.2) (Table 4)

Table 4. Variation of Cd or Cu concentration in urine and hair by grade of G/A ratio. (Protein positive persons)

G/A ratio		0.71 and below	0.72 ~ 1.54	1.55 and over
n		14	11	12
Age		54	61	74
Urine	Protein concentration mg/dl	5.5	4.6	8.5
	G/A ratio	0.4	1.0	2.3
	Cd concentration $\mu\text{g/l}$	4.7	9.6	9.4
	Cu concentration $\mu\text{g/l}$	23	31	53
Hair	Cd concentration $\mu\text{g/g}$	0.5	0.9	0.4
	Cu concentration $\mu\text{g/g}$	13	13	11
	Pb concentration $\mu\text{g/g}$	10	9	5

Remark; the method of quantitative analysis of urinary protein is Kingsbury-Clark's.

1. Increase of Cu concentration in urine is related to G/A ratio.
 2. Cd concentration in urine has tendency to decrease in higher grade of G/A ratio.
 3. Cd, Cu and Pb concentrations in hair have tendency to decrease in higher grade of G/A ratio.
- IV. Comparison of urinary excretive components influenced by tubular

Table 5. Prevalence of β_2 -M G and others in urine in H and N area.
(A random sample)

	Highly-polluted area n=39	Non-polluted area n=56
	%	%
Glucose (+ <)	30.8	23.2
Protein (10mg/dl <)	53.9	41.1
β_2 -M G (10 μ g/ml <)	41.0	3.6
Lysozyme (1 μ g/ml <)	20.5	3.6
T-amino-N (200mg/l <)	30.8	33.9
Age	76.4	74.6

Table 6. Prevalence of Lysozyme positive by aging.
(Urinary glucose positive persons)

Area	Age Sex	50~59	60~69	70~79	80~	Total
		% (n)	% (n)	% (n)	% (n)	% (n)
H	male	0 (9)	0 (7)	69 (14)	87 (8)	44 (38)
	female	0 (7)	29 (13)	76 (25)	62 (6)	52 (51)
	Total	0 (16)	19 (20)	74 (39)	75 (14)	49 (89)
L	male	0 (47)	0 (40)	6 (31)	44 (9)	5 (127)
	female	9 (24)	9 (33)	40 (32)	61 (28)	29 (244)
	Totale	3 (71)	4 (73)	23 (63)	57 (37)	16 (107)

1. Prevalence of β_2 -M G and others positive in urine for at random subjects. (Table 5)

(1) Positive of urine component examined with the way as follows : Glucosuria-testape (+), Protein (10 mg/dl over), β_2 -M G (10 μ g/ml over), Lysozyme (1 μ g/ml over), T-amino-N (200 mg/l over). (2) Subjects were selected at random in population aged 70 years over in H and N areas. (3) The differences of prevalence of Lysozyme and β_2 -M G between H and N area were clear.

2. Prevalence of Lysozyme positive by aging. (Table 6)

(1) Excretion of Lysozyme in urine was increased by aging and was accelerated by Cd pollution.

Table 7. Concentration of β_2 -M G and others in urine.

(Urinary glucose, protein and Globulin positive persons)

Area		Highly-polluted area		Low-polluted area	
Sex		male	female	male	female
Urine	Glucose (mg/dl)	71.6	77.7	70.0	68.2
	Protein (mg/dl)	38.9	36.1	15.3	39.5
	R E P (μ g/ml)	8.0	9.0	1.5	6.0
	Lysozyme (μ g/ml)	0.7	2.7	0.1	1.3
	β_2 -M G (μ g/ml)	27.3	37.0	17.0	32.0
	T-amino-N (mg/l)	249.2	250.4	144.4	206.7
	Proline (mg/l)	0.3	19.2	0.2	3.5
	Cd (μ g/l)	13.7	9.4	6.7	6.7
	Cu (μ g/l)	79.8	62.6	32.6	49.2
	Zn (μ g/l)	322.9	183.6	322.1	222.2
Serum	β_2 -M G (μ g/ml)	3.7	4.0	3.0	3.9
	IP (mg/dl)	3.0	3.1	3.0	3.5

Table 8. Correlation coefficient between Cd and β_2 -M G in urine.

	Sex	Area	n	β_2 -M G	Proline	Lysozyme
Cd	male	H	15	- 0.01	- 0.18	- 0.07
		L	15	0.63**	- 0.07	0.26
	female	H	18	- 0.31	- 0.54*	- 0.26
		L	28	0.32	0.20	0.55**
Cu	male	H	15	0.74**	0.84**	0.93***
		L	15	0.83***	0.51*	0.74**
	female	H	18	0.40	0.67**	0.37
		L	28	0.60***	0.25	0.52**

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ Table 9. Correlation coefficient between β_2 -M G in urine and serum.

	Urine						
	β_2 -M G	Protein	R B P	Lysozyme	T-amino-N	Proline	Glucose
β_2 -M G (Urine)		0.87***	0.76**	0.58*	0.37	0.46	0.61**
β_2 -M G (Serum)	0.43	0.26	0.49*	0.03	0.32	0.31	0.64**

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

Table 10. Cd or Cu concentration in blood, hair and urine.

		Highly-polluted area			Non-polluted area		
		n	Arithmetic $\bar{x}$	Geometric $\bar{x}$	n	Arithmetic $\bar{x}$	Geometric $\bar{x}$
Blood ($\mu\text{g/ml}$)	Cd	34	0.025	0.024	30	0.020	0.018
	Cu	34	0.93	0.93	30	0.94	0.94
Hair ($\mu\text{g/g}$)	Cd	20	0.6	0.5	26	0.6	0.5
	Cu	20	15.8	12.1	26	16.4	13.1
Urine ($\mu\text{g/day}$)	Cd	34	7.9	6.7	30	2.5	2.8
	Cu	34	21.7	19.0	30	12.9	11.6

Table 11. Relationship among Cd or Cu concentrations in hair, urine and blood.

	Area	n	Cd	Cu
Hair Urine	Highly-polluted area	20	- 0.18	0.10
	Non-polluted area	26	- 0.22	- 0.02
Blood Urine	Highly-polluted area	34	0.41*	- 0.07
	Non-polluted area	30	0.49**	- 0.02
Hair Blood	Highly-polluted area	20	0.10	0.09
	Non-polluted area	26	0.11	0.02

* $P < 0.05$, ** $P < 0.01$

3. Comparison of mean value of glucose, β_2 -M G, Cd in urine and β_2 -M G, inorganic P in serum. (Time NO.4) (Table 7)

(1) Subject was persons, who had finding of tubular dysfunction such as glucosuria, proteinuria and G fraction positive by Disc electrophoretic examination simultaneously. (2) It was clear the difference of concentrations of Lysozyme and proline in urine between male and female. (3) It was not clear the difference of concentration of each component between H and L area except proline.

4. Relation of Cd or Cu to β_2 -M G, Proline and Lysozyme in urine. (Table 8)

(1) Cd concentration in urine was not related to those of β_2 -M G, Lysozyme or proline in H area, but it was related to those in L area.

(2) Cu concentration in urine was related to those of β_2 -M G, Lysozyme or Proline in each area.

5. Relation of β_2 -M G in urine or serum to protein, R E P and others. (Table 9)

(1) It is seemed that β_2 -M G in serum is related to tubular dysfunction.

V. Body burden Index.

1. Comparison of Cd or Cu concentration in blood, hair and urine between H and L areas. (Time NO.4) (Table 10)

(1) Cd concentration in blood in H area was higher than that of L area.

2. Relationship among Cd or Cu concentration in hair, urine and blood. (Table 11)

(1) Correlation coefficient between Cd concentrations of blood and urine in H and N area was significant.

DISCUSSION

WASSERMANN (Israel)

Table 3 in your paper indicates a positive age correlation with Cadmium concentration in urine both in low and highly polluted areas. The same appears for Copper in urine in both areas. Since this correlation is positive, only up to age groups of approximately 40 - 49, perhaps these groups of 30 - 39, 40 - 49 years would be most significant for characterizing the urinary concentration of a population in an area.

WATANABE (Japan)

At first it was expected that some effects would be found on the group of 30 - 50, but there were no findings other than an increased Cadmium excretion in urine.

CHAMBERS (Ireland)

Do the differences in excretion showing tubular dysfunction between females and males occur at all times of the menstrual cycle or is there some change during the cycle?

WATANABE (Japan)

We found the difference of tubular dysfunction between male and female on the group of over 70 years old. In view of this, any relation with the menstrual cycle should not be considered.

CLINICAL INVESTIGATION IN NORTHWEST QUEBEC, CANADA
OF ENVIRONMENTAL ORGANIC MERCURY EFFECTS

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ABSTRACT

In 1971, residents of three Cree Indian communities in Northwest Quebec, Canada, were investigated for possible clinical effects of organic mercury. This was done after finding that mercury levels of fish caught in the area ranged to greater than three parts per million.

In the first phase of the investigation, over three hundred persons had blood samples drawn for mercury determination. Many of these individuals had hair specimens for mercury determination collected as well. Approximately half this number had field clinical testing done. Clinical evaluation included full or screening types of history and physical examinations, electro-myograms, and maze performance testing.

Twenty-two individuals were found to have whole blood mercury levels greater than one hundred parts per billion, the highest reading being three hundred and six parts per billion. There was good correlation between hair and blood mercury levels. There appeared to be some relationship between the individual's fish consumption and his blood mercury level. No significant clinical findings suggestive of organic mercury excess were detected.

In the second phase of the investigation, five individuals from one of these communities, four of whom had previously shown

blood mercury levels greater than one hundred parts per billion, underwent extensive in-patient evaluations at the Montreal Neurological Hospital in Montreal, Canada. In addition to routine hospital tests, detailed neurological examinations, as well as electroencephalograms, audiograms, visual field determinations, blood cytogenetic studies, electromyogram and nerve conduction studies, and blood and hair mercury level determinations were carried out.

Here again, no significant clinical findings suggestive of organic mercury excess were detected.

1. Introduction

In the spring of 1971, samples of whole blood from twenty-nine Cree Indians of the Waswanipi band in Northwest Quebec, Canada were tested for mercury by the Federal Department of Fisheries and Forestry (now integrated into the Department of the Environment). This was done after finding that mercury levels of fish caught in the Waswanipi area ranged to over 3 parts per million (ppm). The average mercury level found in the Waswanipi blood samples was 55 parts per billion (ppb) with a high of 135 ppb. It was thus felt necessary to carry out more extensive testing.

In addition, because it was reported that mercury content of fish in Mistassini Lake northeast of the Waswanipi area was quite high, some testing was also carried out amongst the Mistassini band of Indians.

2. Phase I

2.1 Methods

Complete history and physical examinations including specific inquiry about fish consumption, as well as collection of blood for determination of mercury levels, were first carried out in June 1971 on Waswanipi Indians, who are of Cree origin, living in Matagami, Quebec.

These initial history and physical examinations were negative for symptoms and signs of organic mercury poisoning. Therefore a screening battery of tests based on recommendations made at the Symposium on Human Mercury Exposure (held at the Center for Disease Control, Atlanta, Georgia, June 25-26, 1971) was devised to be used for the Waswanipi Indians in the area of Miquelon, Quebec, who were evaluated in July, 1971.

The procedure at Miquelon was to enquire how the individual was feeling. He was then specifically asked about paresthesiae. If there were any significant positive answers to these questions, a complete history and physical examination was carried out. If not, a battery of tests were carried out. This battery included:

- (1) Detection of any hand tremor.
- (2) Testing for dysdiadochokinesia.
- (3) Finger-nose testing with eyes both open and closed.
- (4) Testing of vibration sensation at the ankles with a tuning fork.
- (5) Testing of two-point discrimination of the index finger tips using a paper clip.
- (6) Having the person draw a circle.

- (7) Testing of auditory acuity - first with a watch and if this was positive (not heard), using a tuning fork.

All the above subjects were also questioned about fish consumption. These subjects plus others who did not undergo examinations (particularly school children who spent much of their recent time away from the community) had blood collected for mercury determinations.

The mercury determinations on the blood samples were carried out by the Fisheries and Forestry Department in Montreal using atomic absorption. Portions of six of these samples were sent to the laboratory of Dr. T. W. Clarkson at University of Rochester for independent verification.

These areas were visited shortly thereafter by a technician from the Institute of Environmental and Industrial Health of the University of Michigan who (1) performed electromyograms using a portable apparatus to obtain power spectra plots; (2) administered a maze performance test; and (3) collected hair for mercury determination to be done by atomic absorption at the University of Michigan.

In late July, 1971, a medical student collected blood specimens for mercury determinations from Cree Indians living in Mistassini, Quebec, and in August, 1971, he repeated blood collections in Matagami and Miquelon, Quebec.

It had been hoped that visual field examinations would be performed during the summer of 1971 as well. However, because of problems entailed in obtaining persons competent to carry out such examinations, these were not done until October 1971, at which time they were carried out by two different optometrists - one for Matagami and one for Miquelon.

Advance notice was generally given the community involved that examinations were to be carried out, and virtually anyone who presented himself for testing had it carried out.

2.2 Results

The results are summarized in Table I. Seventy-nine persons at Matagami had blood tested for mercury, ten of these had one or more readings of greater than 100 ppb, the mean was 41.04 ppb and the highest reading obtained was 306 ppb. This latter reading was obtained on a fifty-one year old man in August 1971 (he had had no blood taken in June, 1971). One hundred and forty-one persons from Miquelon were tested, three had readings greater than 100 ppb, the mean was 21.63 ppb and the

TABLE I
Summary of Phase I Evaluation

Test Site	BLOOD MERCURY				HAIR MERCURY		Physical Examinations	Electro- myograms & Nerve Per- formance	Visual Fields
	Number of Persons Tested	Number > 100 ppb	Highest Value Recorded	Mean	Number of Persons Tested	Highest Value Recorded			
Matagami, Quebec (Queenship Band)	79	10	306 ppb	41.04 ppb	11 ✓ $r = 0.82$ with blood values ✓ 56	44.85 ppm	49 full NO	11 SIGNIFICANT	8 FINDINGS
Miquelon, Quebec (Queenship Band)	141	3	148 ppb	21.63 ppb			69 screening 28 full NO	56 SIGNIFICANT	Not done FINDINGS
Micacasini, Quebec (Queenship Band)	181	9	135 ppb	36.76 ppb			Not done	Not done	19 NO SIGNIFICANT FINDINGS

highest reading here was 148 ppb. In Mistassini one hundred and eighty-one persons were tested, nine had readings greater than 100 ppb, the mean was 36.76 ppb and the highest reading was 155 ppb.

Six of the blood specimens collected from Matagami in June, 1971 were centrifuged shortly after collection, so that red blood cell mercury levels could be determined. Portions of these blood specimens were analyzed at University of Rochester while an equal portion was sent to be analyzed by Dr. Magos of the Medical Research Council. There was a reasonably good relationship between the Fisheries and Forestry results and those of Magos.

Eleven persons from Matagami and fifty-six persons from Miquelon had hair specimens analyzed at the University of Michigan. The highest reading, 44.85 ppm was on a specimen from a thirty-eight year old man living at Matagami, who had had a blood mercury level of 172 ppb. A correlation of .82 was found between blood and hair mercury levels.

Full physical examinations were carried out on forty-nine individuals at Matagami and on twenty-nine individuals at Miquelon. Screening examinations were done on sixty-nine individuals from Miquelon. Electro-myograms and maze performance tests were carried out on eleven individuals from Matagami and forty-six individuals from Miquelon. Finally, visual field examinations were carried out on eight of the previously tested individuals from Matagami and on nineteen of the previously tested individuals from Mistassini. In all these clinical examinations no significant findings were detected.

However, there did appear to be a relationship between admitted heavy fish consumption and raised blood mercury levels in that where asked, those individuals with levels greater than 100 ppb admitted to fish consumption more than once per week whereas the majority of individuals stated their fish consumption was once a week or less. Also, with one exception, all those children who had blood specimens collected in early summer 1971 and had attended school in towns away from home for the previous two years or more, had mercury levels of 0 (the one exception had a blood mercury level of 21 ppb).

One final point of interest is brought out in comparing the cumulative blood mercury levels of the first twenty persons from each community who came forward to have blood specimens collected, with the final

twenty. The results suggest that those within a community who came forward first to be tested are less likely to have high mercury levels than those who came forward towards the end of testing.

TABLE II

	<u>Total Blood Mercury (ppb) for Groups of 20</u>		
	Matagami	Miquelon	Mistassini
	<u>(June 1971)</u>	<u>(July 1971)</u>	<u>(August 1971)</u>
First twenty	253	498	496
Final twenty	1115	784	896

2.3 Discussion

It must be pointed out that due to the nature of this field study, valid statistical analysis, particularly of the physical examinations (including visual fields), is virtually impossible to perform. Nonetheless there was no suggestion of any clinical sign or symptom appearing more often than expected within such populations.

The electromyogram power spectra plots were subjected to more rigid statistical analysis, but here too no significant correlation was found with blood or hair mercury levels.

The blood mercury levels done by the Fisheries and Forestry Department appear reasonably valid, both statistically and clinically. They were found to correlate highly with hair mercury levels. Too, a good relationship was found between Fisheries and Forestry red blood cell mercury levels and those done by Magos of the Medical Research Council. And, for further support, there appeared to be a relationship between fish consumption and blood mercury levels.

The reasons why those who first come forward to have their testing done have lower mercury levels than those who come at the end are not clear-cut. However, in general, it seems that women and children tend to come forward first, while the men, particularly those who have been

working or who spend much time "in the bush" tend to come forward last. Possibly, too, those who are more "urbanized" i.e. those who tend to spend more time in the community, utilizing the supplies of the local general store and relying less on natural sources for their food supply thus consuming less fish than the man "out in the bush", are less wary of the outsider.

This point is brought out as a caution for future studies, to ensure that appropriate selection is made when choosing a sample population from within a community. Special efforts might be considered to test individuals out hunting, trapping and fishing in the bush.

More detailed studies of fish mercury levels, carried out in September and October, 1971 revealed that the levels ranged to a maximum of 4.44 ppm in the Waswanipi area and to 0.84 ppm in the Mistassini area.⁽¹⁾

3. Phase II

3.1 Introduction

In that no significant clinical findings were detected in the field studies of Phase I, it was decided to offer some of the individuals with higher mercury levels the opportunity to be investigated more thoroughly.

3.2 Methods

Originally it was hoped to select ten individuals, some with known high mercury levels and others with more "normal" levels, to undergo complete investigation at the Montreal Neurological Hospital in Montreal, Quebec. However, due to uncontrollable circumstances, only five persons were investigated, four of whom had previously shown blood mercury levels of greater than 100 ppb and one who had not previously been tested. At the time of the investigation, these individuals were aware that high mercury levels had been found in the area, but were not yet aware whether they themselves were amongst those who had the higher levels.

All testing was carried out on an outpatient basis within an interval of five days in February, 1972. Use was made of two Cree Indian interpreters. The following procedures were carried out:

1. Complete medical and neurological examinations - performed by a neurology resident of the hospital.
2. Psychological testing - performed by hospital psychologists.

It must be stated that this aspect of the evaluation created

(1) Unpublished data, Environment Canada.

the most difficulties, as there were inadequate norms from which to work and the language barriers were virtually insuperable despite the presence of the interpreters.

3. Electromyogram and nerve conduction studies.
4. Electroencephalograms.
5. Audiograms.
6. Visual field determinations.
7. Cytogenetic studies - in which blood was drawn at the hospital and sent to the Health Protection Branch of National Health & Welfare in Ottawa for analysis.
8. Blood and hair mercury levels - specimens being collected at the hospital and sent to the same department as in No. 7. Blood mercury levels were determined using atomic absorption - while hair mercury levels were determined utilizing neutron activation.

Routine hospital tests done included:

9. Chest X-rays.
10. Hemograms.
11. Complete Urinalyses.
12. SMA - 12

3.3 Results and Discussion

Details of the persons investigated and their findings are available upon request to the author. (See appendix)

Although non-specific abnormalities of the type expected within such a population were, of course, found, no significant clinical findings suggestive of a chronic effect of mercury were seen. Electromyography, electroencephalography, visual fields, and blood cytogenetics are all normal in those persons with the elevated mercury levels.

4. Conclusions

1. Some moderately elevated blood mercury levels have been found amongst Indians of the Waswanipi and Mistassini Bands.
2. There is a satisfactory correlation of blood and hair mercury levels in the studies done.
3. There appears to be some relationship between an individual's fish consumption and his mercury level.
4. No significant clinical findings suggestive of organic mercury excess have been detected.

Results of Studies on Residents
at Montreal Neurological Hospital
for Environmental Organic

Subject Number	Birth Date	Blood Mercury Levels (ppb)			Hair Mercury Levels (ppm)		General Physical Abnormalities	Neurological Abnormalities	Electromyography	Electroencephalogram
		June 1971	Aug. 1971	Feb. 1972	June 1971	Feb. 1972				
(1)	1914	227-RBC 17-plasma	187	43	26.10	29.2	None	None	Normal	None
(2)	1921	—	306	105	27.50	58.7	Traumatic amputation of right forearm below elbow. Persistent crepitations--both lower lung fields. Grade II/VI systolic ejection murmur best heard along left sternal border. Perforated right tympanic membrane.	Slight terminal tremor on left finger-nose testing.	Normal	None
(3)	1909	73	127	23	0.94	20.8	Left leg shorter than right (apparently congenital). Left hydrocele. Both tympanic membranes perforated.	None	Normal	None
(4)	1933	—	172	111	44.85	49.8	Obese	Weakness and slight wasting of muscles of right leg. (History of acute episode to right leg 27 years previously.)	Normal	None
(5)	1895	—	—	11	—	16.8	Systolic hypertension. Systolic ejection murmur along left sternal border. Cataracts.	Mild generalized muscular wasting. Rombergism. Rather slow/rapid alternating movements. Slightly decreased ankle vibration sensation.	Suggestive of right carpal tunnel syndrome.	None

of Studies on Residents of Matagami, Quebec
 eal Neurological Hospital in February, 1972
 Environmental Organic Mercury Effects

Neurological Abnormalities	Electromyography	Electro-Encephalography	Audiogram	Visual Field	Blood Cytogenetics	Chest X-ray	Hemogram Abnormality	Urinalysis	SMA 12 Abnormal Values (Normals in parenthesis)
None	Normal	Normal	Impedance testing satisfactory. Air conduction threshold testing abandoned because of language barrier	Normal	Within normal limits	Normal	Hemoglobin 11.7 Smear moderate hypochromia Sed. rate 32	Satisfactory	Normal
Slight terminal tremor on left finger-nose testing.	Normal	Normal	Right middle-ear pathology.	Normal	Within normal limits	Evidence of pleural thickening, calcified granulomas and bronchiectasis	Normal	Satisfactory	Normal
None	Normal	Normal	Bilateral middle-ear pathology.	Normal	Within normal limits	Scoliosis	Normal	Satisfactory	LDH 428 (100-350)
Weakness and slight wasting of muscles of right leg. (History of acute episode to right leg 27 years previously.)	Normal	Normal	Mild high frequency sensorineural loss on right - normal otherwise	Normal	Within normal limits	Calcified granulomas - right middle lobe	Sed. rate - 38	Satisfactory	LDH 402 (100-350) Alkaline phosphatase 18.2 (3-12)
Mild generalized muscular wasting. Rombergism. Rather slow/rapid alternating movements. Slightly decreased ankle vibration sensation.	Suggestive of right carpal tunnel syndrome.	Normal	Moderate bilateral sensorineural hearing loss.	Normal	Within normal limits	Cardiomegaly	Sed. rate - 47	Albuminuria 20-70 pus cells in clumps	BUN 24 (10-20) LDH 408 (100-350) *LDH results were generally relatively high in this hospital laboratory.

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5. Recommendations

1. Blood and/or hair should be screened for mercury periodically in areas where high environmental mercury levels are found.
2. In screening individuals, special effort should be made to obtain specimens from individuals who have spent much time outside of their settlement, fishing, trapping and hunting.
3. Detailed clinical evaluations should be offered to selected individuals with higher mercury levels.
4. Open and frank communication with individuals and groups being evaluated should be encouraged.

DISCUSSION

DANIELSON (Sweden)

1. Was mercury in fish measured as organic mercury?
2. What was the average mercury level in fish?
3. Was fish consumption measured in more specific terms, e.g. g/day?

BERNSTEIN (Canada)

1. No, not in the specific studies referred to in the paper. It is generally accepted however, on the basis of investigations conducted elsewhere that the majority of mercury present in fish muscle is methylmercury.

As mentioned in the paper, six blood specimens were centrifuged to separate the cellular fraction. In these specimens the majority of mercury was found in the red cell fraction, lending support to the concept that one was dealing predominantly with organic mercury.

2. In the Waswanipi area, average whole mercury fish levels ranged from 0.16 ppm to 1.98 ppm depending on the species of fish and the body of water tested.

In the Mistassini area the average levels ranged from 0.25 to 0.60 ppm.

3. No, not in this study. In a few instances where this has been attempted, under comparable circumstances, the information derived has not been very satisfactory.

BRAMAN (U.S.A.)

Did you determine if the source of environmental mercury pollution (prior to absorption by fish) was actually inorganic or organic mercury?

BERNSTEIN (Canada)

No, not in this study. Sources in comparable situations elsewhere in Canada would appear to be predominantly inorganic mercury.

It must be pointed out that natural sources of mercury (as contrasted to man-made sources) seem to play a significant role in the total environmental mercury level found in regions such as those we studied.

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SCALING OF ANNOYANCE IN EPIDEMIOLOGICAL STUDIES

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ABSTRACT

The measurement of annoyance evoked by environmental agents often involves survey techniques. Specific problems, such as effects of response criteria and comparability between population responses, are not well solved by using the assumptions behind the traditional survey methods. In criteria work the meaningfulness and effectiveness of such data are critical, strongly underlining the need for improvements of the methods. The introduction of modern scaling techniques into surveys can give the necessary improvements. Investigations on general annoyance with regard to pulp mill odors and aircraft noise demonstrate that it is possible to measure the population response criteria as well as the population response as such. Guidelines are given for annoyance measurements that result in calibrated measures permitting comparisons between differently exposed areas, that fulfill the assumptions for commonly used statistical procedures, and thus enable the determination of meaningful dose-response relationships.

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1. Introduction

A recurrent task in environmental research and community planning is to measure annoyance evoked by environmental agents in the community. The typical tool has been the sociological survey from which dose-response relationships have been constructed for e.g., community noise (e.g., Traffic Noise in Residential Areas (1); Rylander, Sörensen & Kajland (2); Patterson & Connor (3)).

In an annoyance survey, usually a representative group of persons is presented questions on annoyance with several well defined response categories. Two principle approaches are common for estimating the annoyance with regard to an environmental agent; either (1) a battery of questions constituting a Guttman-like attitude scale to obtain annoyance scores or (2) self-rating questions to obtain direct annoyance estimates. Both approaches were employed for example in the Heathrow studies (McKennell (4)). This paper will not deal with attitude scales but the measurement of degree (intensity) of annoyance as expressed in responses to self-rating questions.

Traditionally, the results of the self-rating questions are treated in two different ways depending on whether the aim is to measure the extensity of annoyance (cf. Galloway & Jones (5)) or the mean degree of annoyance in the population. The extensity of annoyance is determined by simply calculating the proportions of persons responding in certain categories (e.g. Rylander, Sörensen & Kajland (2); Patterson & Connor (3)). Such proportions are sometimes regarded as a sufficient basis for dose-response descriptions. If instead the mean degree of annoyance is to be quantified, category scaling has been utilized (e.g. Grandjean et al. (6);

McKennell (7)).

Annoyance surveys are mostly conducted in populations chronically exposed to the agent in question. This circumstance always limits the generalization of results for criteria work. The responses from exposed individuals may be biased due to the exposure itself, differences in attitudes, and other so called extra-expositional factors, i.e. their response criteria² may differ from the criteria of the non-exposed individuals. Similarly, the response criteria for populations exposed but to a varying degree may differ (see e.g., Thibant & Kelly (8)). This problem has been noticed in the laboratory (Borsky & Leonard (9)) as well as in the field (McKennell (10)). To obtain comparability between differently exposed populations the variation of the response criteria must be known and, if necessary, corrected for.

Psychophysical scaling research has developed quantitative methods suitable for measuring the degree of annoyance with regard to environmental agents in such a way as to permit a satisfactory control of the response criteria variation (for a review of these methods see Ekman & Sjöberg (11)). The present team has demonstrated the applicability of psychophysical scaling methods in the annoyance survey. The emphasis is put on the measurement of mean degree of annoyance and the need for calibration procedures; these seem to be two critical factors arising when annoyance responses are compared or a prognosis is made of the annoyance in the community.

²Response criteria are here defined as the respondents- locations of the response-category boundaries on the continuum of annoyance.

2. Theoretical Considerations

When self-rating questions are chosen for annoyance surveys many investigators utilize only a small amount of the information contained in the survey data. The proportions of persons in the response categories above an arbitrary cut-off point are lumped together, disregarding the distribution of the respondents over the categories. This way of utilizing the data is illustrated in Fig. 1 for a 7-category scale where the cut-off point is set at the 4th category boundary. The cut-off point could for example dichotomize the respondents into "little annoyed", and "much annoyed" persons. The main question is to what extent the proportion of "much annoyed" persons represents not only extensity but also the intensity of annoyance. In the following, three theoretical models of measurement are discussed with regard to their appropriateness to estimate extensity as well as intensity of annoyance.

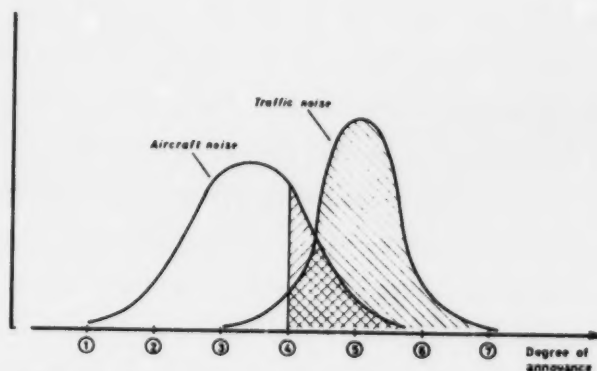


Fig. 1. Theoretical frequency distributions of annoyance evoked by aircraft noise and traffic noise. The shaded area shows the proportion of persons more annoyed than is represented by the 4th category boundary.

2.1 Model 1

The assumptions behind the traditional treatments and uses of survey data are rarely discussed in the literature from a measurement point of view. The unspoken but basic assumption can be stated as follows: All persons, not only within an area but also between differently exposed areas, use fixed response criteria. This assumption is illustrated in the left diagram of Fig. 2 (Model I) where hypothetical distributions of responses to, e.g., traffic noise, are shown for two differently exposed areas, A and B. The shaded part of the distributions represents the proportion of persons that respond in annoyance categories above a certain boundary (here the 4th) on a verbal category scale. The critical question is whether the cut-off point is fixed and equal in Area A and B. This is a necessary condition even if the extensity of annoyance is to be measured. Moreover, the choice of the cut-off point, i.e., its location on the annoyance scale, is more or less critical depending on the form and location of the response distribution.

Although Model I is frequently used for determining the extensity as well as the intensity of annoyance, several factors critical for the validity of the basic assumptions are reported in the literature. For example, acclimatization towards greater tolerance to the exposure conditions (McKennell (7)) can be one such factor. Also, the findings of Hazard (12) and Grandjean et al. (6) indicate a dependence between annoyance response to the target agent and the exposure conditions in general. Demonstrated differences in the interpretation of the phrasing of questions and category labels constitute another factor (cf. Jones & Thurstone

(13); Jonsson (14). Further, practical experience has shown that induced changes in attitudes may be accompanied by drastic changes in proportions of annoyed persons (Sörensen (15)). Such results may reflect not only a change of degree of annoyance response to an environmental agent but also a dislocation of the response criterion.

2.2 Model II

The center diagram of Fig. 2 illustrates Model II where the 4th category boundary is assumed to be fixed within an area but differs between areas in terms of degree of annoyance. In this hypothetical example, the 4th boundary represents a higher degree of annoyance in Area B than in Area A. If the 4th category boundary is chosen as the cut-off point the proportion of annoyed persons will be the same in both areas. When the comparison is made on equal terms, i.e. at the same degree of annoyance, the proportion of annoyed persons is higher in Area B. Thus, if there is a difference in response criteria between areas they should be compared with respect to the same cut-off point on the annoyance scale, regardless of the verbal labels of the response alternatives. To do this, a calibration of the underlying annoyance scales must be made.

2.3 Model III

If the meaning of the 4th category boundary varies between and within areas, the measurement problem becomes even more complicated. An illustration of Model III is presented in the right hand diagram of Fig. 2. The distribution to the left represents the annoyance felt by a population in response to a disturbance and the distribution to the right represents the annoyance associated with the 4th

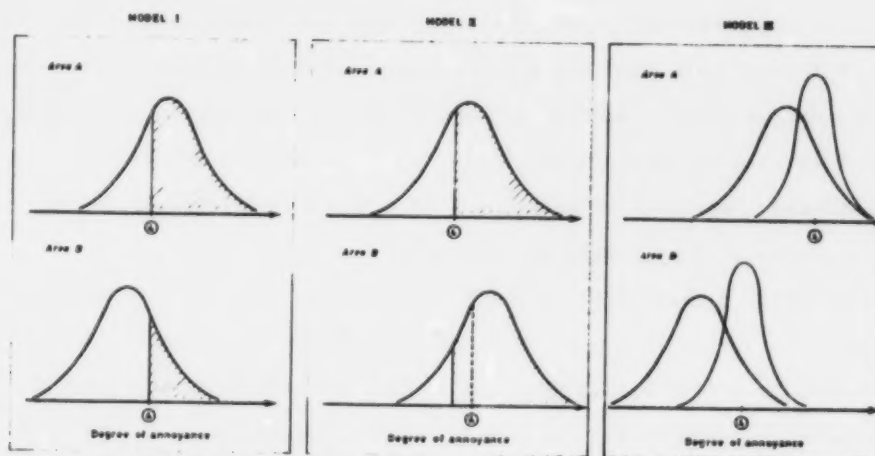


Fig. 2. Models for three different views on response criteria in differently exposed populations.

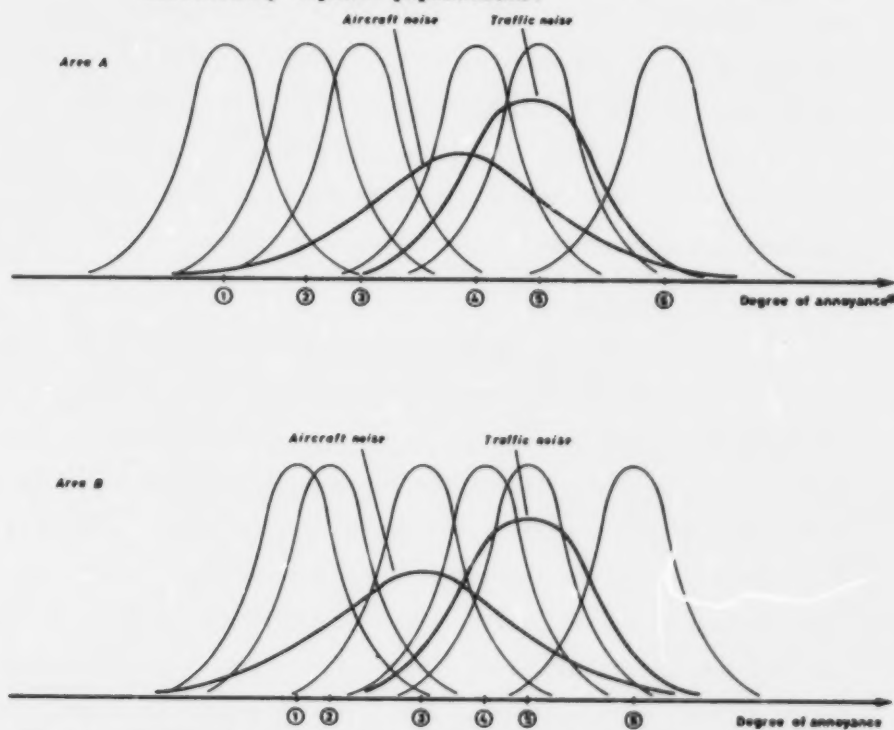


Fig. 3. Theoretical frequency distributions of annoyance evoked by aircraft noise and traffic noise (thick lines) in two differently exposed areas. The distributions of the category boundaries are also shown (thin lines).

category boundary. Both distributions contain the same individuals. It follows that when Areas A and B are compared, simple proportions cannot be used. Accordingly, if Model III describes reality it is impossible to obtain a measure of the extensity of annoyance. Instead comparison of areas must be made in terms of calibrated measures of mean degree of annoyance.

Fig. 3 shows Model III with hypothetical annoyance agents (aircraft and traffic noise) together with the set of response alternatives to a self-rating question. The two agents as well as each category boundary give rise to response distributions. The distances between the category boundaries are allowed to vary within as well as between areas. It should be stressed that according to the model the response given by each individual depends not only on the degree of annoyance evoked by the environmental agent but also on his response criteria, i.e. where he locates the category boundaries. By Thurstonian scaling of responses to self-rating questions all the information collected is utilized.

3. Empirical Studies

In the following the three theoretical models (Fig. 2, Models I-III) are applied to data from self-rating questions on annoyance collected in surveys on pulp mill odors and aircraft noise. The stress is put on the applicability and meaningfulness of the models rather than on any specific dose-response relationship. A detailed presentation of the two surveys is given elsewhere (Berglund, Berglund, Jonsson & Lindvall (16), Berglund, Berglund & Lindvall (17)). Both surveys covered differently exposed subareas. The questionnaires included items on "annoyance in general" with regard to several environmental agents. The respondents were to rate their annoyance

on verbal category scales with 6 or 7 categories (cf. Fig. 3).

3.1 The Traditional Approach

Model I is implicit in the traditional treatment of data for estimating the extensity of annoyance. The model requires that the response criteria corresponding to the cut-off points are fixed both within and between areas. A cut-off point is thus assumed to represent the same degree of annoyance in all the areas compared. In Fig. 4 results are shown for the two self-rating questions on annoyance treated according to Model I. Two cut-off

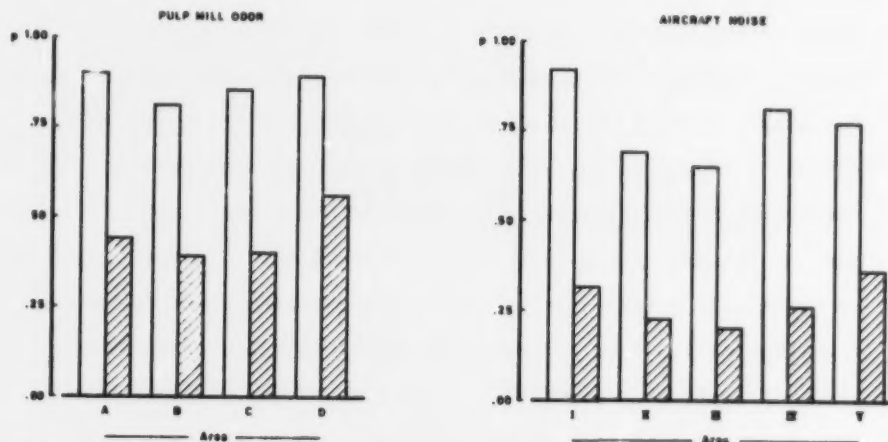


Fig. 4. Proportion of annoyed persons responding to a question on general annoyance in two surveys. The open and shaded bars represent the results when two different category boundaries are used as cut-off points. (Sample sizes 76-175 persons).

points have been chosen for the illustration: One representing all responses including and above "fairly little annoyed" (open bars) and the other including and above "fairly much annoyed" (shaded bars).

The results for both the odor and the noise questions show that the rank orders of the areas are not identical for the two cut-

off points. Even though the differences in extensity of annoyance are small, this is the expected outcome if the response distributions differ between areas. That response distributions can vary with the exposure to community noise has been demonstrated nicely by Boraky & Leonard (9). Mainly for the theoretical reasons presented we are inclined to abandon Model I and to strive for models of measurement that require less rigid assumptions.

3.2 Alternative Approaches

In Model II and III the locations of the verbal categories along the annoyance continuum are allowed to be different among areas. In Model III, this location may also vary within the areas. These conditions are illustrated in Fig. 3. The measurement approach to satisfy Model II is limited to a calibration of the underlying annoyance scales so that the verbal response categories are comparable. It should be stressed that a calibration cannot be made on the proportions directly. Therefore a solution according to Model III is imperative. Model III requires a mathematical treatment of the data according to Thurstone's Law of Category Judgment (see Torgerson (18)). The specific assumptions behind the solutions applied are that the variances of each response category boundary are constant and independent of the specific environment agents.

In the treatment of the collected data on "annoyance in general" with regard to pulp mill odors and aircraft noise, the least rigid model, i.e. Model III, has been used. It should be noted that Models I and II are special cases of Model III so that a solution according to Model III will also be a solution of Model I and II.

Thurstone's Law of Category Judgment demands that the frequency

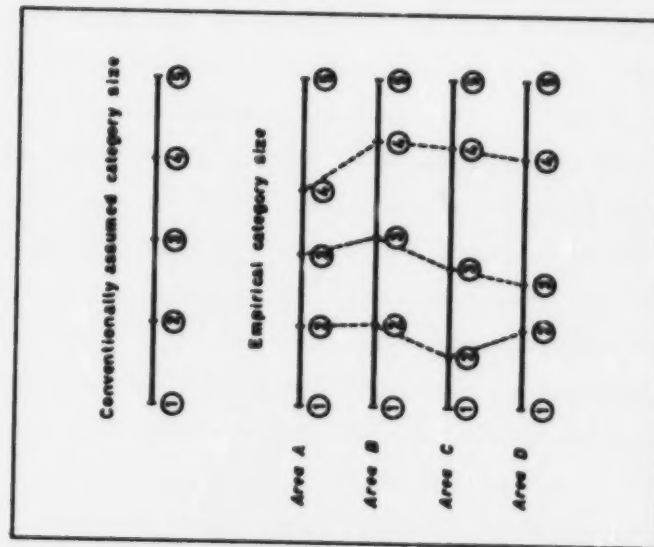
of response be tabulated for each environmental agent for each response category. This frequency is then transformed to a proportion of the total number of responses. The proportion is further transformed into a normal deviate. It is from the normal deviates that the continuum of annoyance can be derived (Gulliksen's method of least squares; cf. Torgerson (18)). Once the annoyance scale is established, locations of the boundaries for the verbal categories and the environmental agents are easily determined. Single annoyance values are obtained for each agent and category on the same interval scale of annoyance. The interval property of the scale means that the annoyance scales for different areas can be calibrated to a common reference point and a common unit of measurement.

3.2.1 Scales of Response Category Boundaries

The Thurstonian scaling of annoyance in the two surveys gives the locations for the category boundaries that are presented in the lower part of Fig. 5. The upper parts of the diagrams present the conventionally used response model for self-rating questions (e.g. Borsky & Leonard (9); Grandjean et al. (6)). It simply states that the interdistances between the category boundaries are of constant size. Obviously the empirically obtained category interdistances are unequal within as well as between areas for both the surveys.

The fact that the category sizes vary between areas invalidates the use of proportions of persons above any response category (cf. Model I) as a measure of extensity of annoyance. The result that the category sizes are unequal is by no means unexpected. For example, in well controlled laboratory experiments adverbs of degree (e.g. slightly, quite, very) have been shown to produce

PULP MILL ODOR



AIRCRAFT NOISE

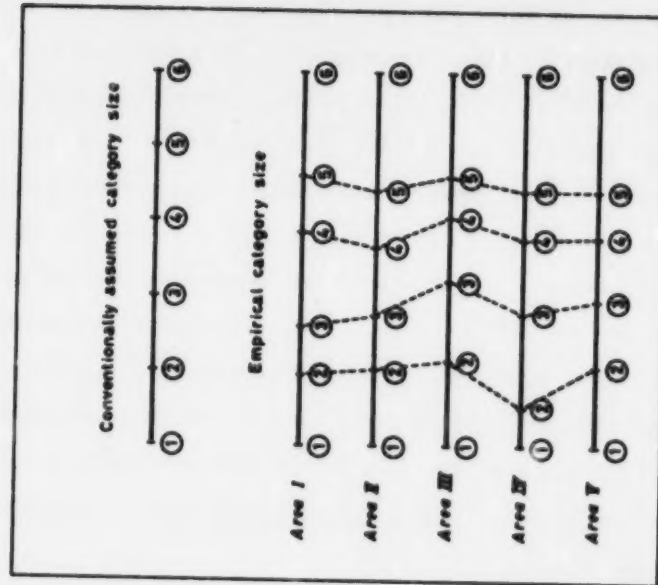


Fig. 5. Thurstonian scales of the category boundaries from two surveys. For comparison the conventionally assumed locations of the category boundaries are shown in the upper part of the diagrams.

unequal steps when used as modifiers of an adjective (e.g. "annoyed") (Cliff (19); for survey data see McKennell (10)).

3.2.2 Calibrated Scales of Annoyance to Environmental Agents

The Thurstonian scaling method provides annoyance measures of both response category boundaries and environmental agents on interval scales. However, direct comparisons of annoyance responses between different areas require a calibration of the scales. This means, as stated earlier, that the annoyance scales must be transformed to the same unit of measurement and to a common reference point. There are several possible ways to do this calibration. Common to all of them is that at least two reference anchors have to be included in the survey. In the present investigations the following anchors were tried: (a) annoyance evoked by an experimentally introduced reference stimulus (standard odor or standard noise) and (b) annoyance evoked by the traffic noise in a nearby city. The units of measurement were defined as the distances between the two anchors on the scale, the anchors also serving as the common reference point. The choice of anchors is merely an illustration of the calibration principle and should not be regarded as a recommendation of specific anchors.

The usefulness of Model II can be illustrated by the calibrated annoyance scales. In Fig 6, left hand diagram, the results of the aircraft noise question treated according to Model II are shown for areas comparable from a noise exposure point of view (take-offs only). In the figure frequency distributions of the annoyance responses with regard to aircraft noise are drawn. The curves are obtained from normal ogives fitted to the cumulative proportions and the annoyance scale values. For illustration a cut-off point is set at the same degree of annoyance value for all areas, N.B. not

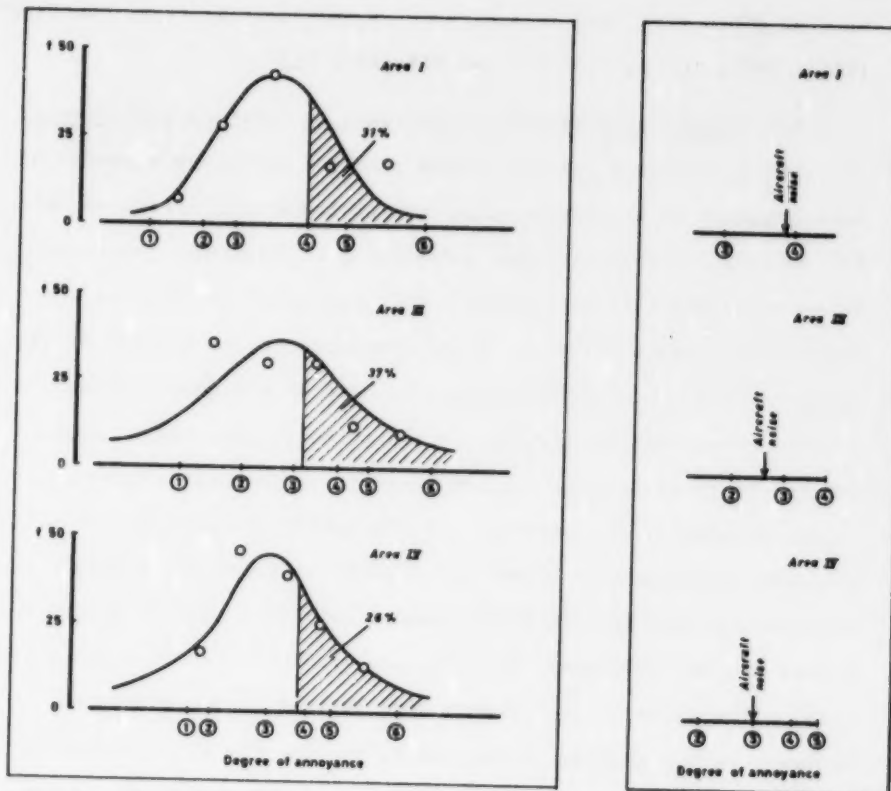


Fig. 6. Thurstonian scales of "annoyance in general" with regard to aircraft noise for three differently exposed areas. The left hand diagram shows obtained frequency distributions of annoyance. The shaded parts of the distributions show the proportion of the populations that are more annoyed than is represented by the cut-off point. The right hand diagram shows the mean degree of annoyance with regard to aircraft noise in the three populations. All scales are calibrated, allowing comparisons between areas.

at a certain verbal category boundary (cf. Fig 2, Model I and II).

The results in Fig. 6 show the proportion of persons that are more annoyed than the degree of annoyance represented by the cut-off point (shaded part of the curve). Being obtained from calibrated scales, the proportions in the different areas are comparable on equal terms. Calibrated scales are a minimum requirement

if administrative decisions are to be based on proportions of annoyed persons.

Another tactic is to measure the mean degree of annoyance evoked in the population by the environmental agent. Such annoyance studies have been performed earlier but we have not found any case where Model III has been applied. Instead, Model I has been used that requires equal category sizes on the response scale; however, in doing so Borsky and Leonard (9) have clearly pointed out the problem with incomparable scale units. Direct measurement of degree of annoyance is possible to perform on the traditional survey data provided the sample sizes and number of response categories are large enough. The results from such an analysis (Model III) are presented in Fig. 6, right hand diagram. The data are from the aircraft survey. The annoyance scales are calibrated in the same way as was done in the left hand diagram. As is evident from the figure, the "aircraft noise in general" is most annoying in Area I, less annoying in Area III and least annoying in Area IV just as would be expected from the physical exposure point of view.

Moreover, by the same technique (Model III) it is possible to compare the degree of annoyance for several environmental agents both within and between areas provided the proper calibration procedures have been applied. This possibility is illustrated by the empirical results from one of the areas in the aircraft noise investigation, in Fig. 7. The curves are fitted by the same procedure as in Fig. 6. In this specific area "aircraft noise in general" was shown to be less annoying than the reference anchors. The degree of annoyance for each agent is expressed by the mean of the distribution. These means are located on an interval scale of annoyance and therefore quantitative comparisons are possible.

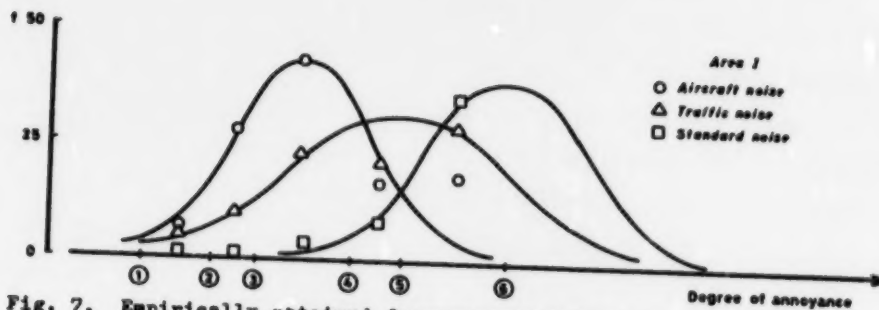


Fig. 7. Empirically obtained frequency distributions of annoyance with regard to three different noises. The means of the distributions represent the degree of annoyance.

3.2.3 Concluding Remarks

It has been demonstrated that the extensity approach of treating annoyance data in terms of proportions gives uncertain information about the mean degree of annoyance. Even if a supplementary calibration of annoyance scales for the different areas is made, the proportions may still be useless for prognosis purposes. This stems from the fact that if we admit the existence of response criteria variation it is impossible to say precisely how much a certain change in physical exposure will change the proportion of annoyed people. However, if instead the mean degree of annoyance to the disturbance factor is actually measured on a calibrated interval scale, then a meaningful dose-response relationship can be established. Only then can precise recommendations be given e.g., as to how much the exposure level has to be reduced in order to meet established ceiling limit values with respect to population annoyance.

Before extensity of annoyance according to Model I could be considered for decisions in community planning and investment proof would have to be presented that the basic assumptions are realistic. But it should also be noted that by increasing the sophistication in the data treatment the requirements put upon the underlying assumptions become more lenient. From this point of view the

application of Model III is safest in practical work. Further, the appropriateness of the basic assumptions for all the three models can be checked only by solutions based on Model III.

4. Guidelines for Improvements of the Annoyance Survey

The following recommendations are given for improvement of annoyance scaling based on self-rating questions in epidemiological studies. The recommendations are given primarily from a psychometric point of view.

First, whenever economically possible Thurstonian scaling should be used to determine the mean degree of population annoyance. Second, to permit such a scaling the questionnaire must include a large number of response categories (at least 6), preferably using only adverbs of degree as modifiers of the annoyance adjective. Third, the survey should include questions on the annoyance evoked by several environmental agents, not only by the target factor. Fourth, to allow for a satisfactory data treatment subsamples of respondents must be comparatively large; ideally at least 200 persons are needed in each subsample to get a reliable population measure of annoyance. Fifth, if areas or populations are to be compared, the annoyance scales must be calibrated. Such a calibration is particularly necessary when annoyance responses to different environmental agents are to be determined. To achieve this at least two reference anchors have to be introduced into the survey. There is a strong need for development of suitable reference anchors for practical work.

ACKNOWLEDGMENTS

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DISCUSSION

(Editorial Comment: the following discussion represents a considerable expansion of the exchange of views which took place orally).

RYLANDER and SÖRENSEN (Switzerland)

The paper "Scaling of annoyance in epidemiological studies" presented by Berglund et al concerns methods to assess the presence of annoyance reactions in populations exposed to environmental agents. The authors criticize the conventional methods, mainly because of a postulated variation in response criteria and propose the use of a method involving Thurstonian scaling to evaluate annoyance.

The following presents a critical analysis of the paper. Initially the traditional social survey method for the determination of annoyance will be reviewed, whereafter the paper by Berglund et al will be discussed.

Measurement of annoyance

Annoyance due to environmental agents may be generally defined as "a feeling of displeasure associated with any agent or condition realized or believed by an individual or a group to be adversely affecting them" (Borsky 1972).

In exposure to single events the momentary reaction can be defined as acute annoyance. When a collection of individuals is exposed to several events over a longer time period, certain individuals might experience chronic annoyance.

The chronic annoyance reaction is related to activity disturbances caused by the exposure. It is also dependent on extra-expositional factors such as the susceptibility of the individual, socio-economic conditions and attitudes. Due to the influence of these factors the relation between individual annoyance and the exposure level is never very high (e.g. Hazard 1971). The relation between the exposure and the mean reaction in a sufficiently large group of the population is however precise and the reproducibility is good (Alexandre 1974).

To study the extension of annoyance in a population, social survey methods are used. They must be performed according to several criteria which have been well defined. For instance, in order to prevent the respondent from consciously exaggerating or underestimating his annoyance, the reason for the investigation must be masked. Questions on the specific agent studied have to be included in a battery of questions on other agents in the vicinity. The choice of the verbal expression for annoyance is also important (Jonsson 1964).

The annoyance is usually expressed in various degrees - little annoyed, rather annoyed, very annoyed or as various steps on an annoyance scale, or a multiple question index. The distribution of the various degrees of annoyance in a population is not normal and the intervals between the various degrees are unequal (Jonsson and Fog, 1968). It has been shown that the highest degree of annoyance is best related to the level of the exposure agent. Lower degrees of annoyance are more influenced by extra-expositional factors and thus less suitable for the construction of dose-response relationships (Rylander et al 1972a, Sörensen et al 1974).

Discussion of Berglund paper

In their presentation Berglund et al discuss the possibility that the response criteria for persons expressing annoyance may be different between areas with different exposure levels or in newly exposed areas. In principle the points raised are important and should be evaluated against information available in the literature.

Concerning the variation in response criteria between areas with different exposure levels available data seem to contradict this hypothesis. Alexandre (1974) and Rylander et al (1972b) demonstrated close dose-response relationship for a large number of areas exposed to varying levels of aircraft noise. The same consistency has largely been found for traffic noise in English and French investigations.

As a support for the hypothesis that response criteria will vary Berglund et al discuss acclimatization to the agent, a dependence to the agent, phrasing of the questions and attitudes.

All this represents well known phenomena (Borsky 1972) and the traditional social surveys are designed so that the influence of these factors is minimized.

The problem concerning reactions in exposed and non-exposed areas is of particular importance for prognostic purposes. Experimental data are available also on this aspect. Jonsson et al (1974) reported data from annoyance due to oil refinery odors and noise from traffic, shooting ranges and aircraft. They compared the prognostic values on annoyance based upon field studies around similar locations with values found when the real exposure situation has been established. The agreement was found to be very good. These results do not support the theory that the variation between non-exposed and exposed areas would be of importance for the accuracy of planning.

To test the possibility of varying response criteria in areas with different exposure levels, Berglund et al use data from field surveys on odors and aircraft noise. They group the annoyance data from different areas in these studies into two categories: "fairly little annoyed and more" and "fairly much annoyed and more".

They found in figure 4 in their paper that the ranking order of the areas is different for the two categories of annoyance. From this they conclude that the response distribution differs and that the response criteria vary between areas. In their report they are not, however, using the relevant annoyance data from the studies they cite. The annoyance has been assessed using a question on annoyance constructed by the authors themselves. The usual question "how much annoyed are you?" reflects the individual's experience in his actual exposure situation. The question "what do you think about aircraft noise in general?" constructed by Berglund et al, has no reference to the particular exposure situation of the individual. The criteria for annoyance studies as referred to in the previous section have thus not been adhered to.

If instead the relevant annoyance data from the studies are used, it is seen that the ranking order between areas is not different for the various groups of annoyance (Table 1). Rankings for different categories of annoyance has also been evaluated in all areas in the investigation from which Berglund et al have chosen 5 areas. The results are shown in Table 2.

It is seen that by and large the ranking order for the two groups of annoyance are similar. Differences in ranking order are present between two groups of areas. The differences for the percentages are however very small and within the accepted variation.

The data analysis presented by Berglund et al to support their hypothesis must therefore be rejected.

Epilogue

Even if it is not possible to prove the hypothesis presented by Berglund et al concerning the shortcomings of the traditional methods for the study of annoyance, it is still of interest to discuss their proposals for improved social surveys.

They recommend the utilization of all degrees of the annoyance response to construct an average annoyance level. As only the highest degree of annoyance is well correlated to the exposure level (see section on measurement of annoyance), this approach seems to be less valuable.

The second proposal is the correction of the annoyance using "reference anchors". This would be an interesting approach if verbal differences were present in the expression of annoyance reaction. This has not been demonstrated.

The correction procedure requires that the distance between the anchors is identically evaluated by all individuals in the study. Concerning the examples for anchors "how to you consider traffic noise in the city during rush hours", this reference point - in the absence of any data on its validity - seems to be even more influenced by experience and extra-expositional factors than the traditional questions on annoyance criticized by the authors for this reason.

The second anchor involves an evaluation of an acute exposure to noise or odors. It has earlier been shown that the exposure to acute stimuli correlates better to the physical noise level than to chronic annoyance (Borsky 1974). Thus this anchor does not appear to be useful.

In view of the above, it seems difficult to postulate that the distance between the two anchors will be constant, until experimental data have been produced which demonstrate this.

Other anchors might be more useful but in the absence of any suggestions and data to demonstrate their validity this will remain speculative.

Conclusion

Social survey methods are incomplete in many ways. It would be especially desirable to increase the accuracy for the expression of the annoyance reaction in the community, as well as make it possible to use the reaction of the individual rather than a group mean. The paper presented by Berglund et al contains many interesting ideas. In view of the absence of data which prove their validity they will remain speculative and do not present a support for the conclusions found in the paper.

Table 1

Extent of annoyance (%) and ranking order (R.O.) between different areas in odor/aircraft noise studies using relevant data for the different groups of annoyance.

AREA	LITTLE ANNOYED OR MORE		RATHER ANNOYED OR MORE	
	%	R.O.	%	R.O.
Aircraft noise				
MMA 3	41	1	13	1
MMA 2	18	2	12	2
MMA 5	12	3	6	3
MMA 1	9	4	5	4
MMA 4	6	5	3	5
Odor				
BBY 1	93	1	72	1
BBY 2	84	2	65	2
BBY 3	49	3	34	3

Table 2

Extent of annoyance (%) and ranking order (R.O.) between areas with different exposure levels to aircraft noise (data from Rylander et al 1972).

AREA	LITTLE ANNOYED OR MORE		RATHER ANNOYED OR MORE	
	%	R.O.	%	R.O.
OSL 6	78	1	70	2
OSL 4	73	2	71	1
OSL 5	67	3	66	3
CPH 5	62	4	60	4
CPH 4	55	5	55	5
OSL 2	48	6	44	6
OSL 3	47	7	45	7
CPH 6	40	8	40	8
CPH 3	22	9	18	9
CPH 2	13	10	11	10
CPH 1	12	11	12	11

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BERGLUND (Sweden)

The comments of Dr. Rylander made during the session have later been changed and considerably expanded. Accordingly, I am forced to give a more elaborate answer than I gave in the session.

1. One of the main objectives of the present symposium has been the concern for improvements of methodologies. Our paper presents a new psychophysical approach applicable in the annoyance survey. Therefore, I am surprised by Dr. Rylander's negative reaction to our paper. I cannot understand how our suggested improvements of methodology could be harmful to the annoyance surveys.

2. To avoid misunderstandings I will repeat the main points of our paper. These are:

- to openly display the assumptions behind different methods of annoyance assessment,
- to clarify the requirements of the annoyance measurement methods before they can be used in the construction of precise dose-response functions, and
- to recommend the use of calibration procedures and to suggest how such calibrations can be done.

Although the methodological problems brought up by us may have implications for specific investigations, I will restrict myself to respond on materials presented in this session.

3. Dr. Rylander argues that we criticize the conventional measurements because of a postulated response criteria variation. We do not postulate such a variation but base our view on empirical evidence presented by us and other researchers. The full references are given in our paper. Dr. Rylander refers to the same findings and underlines the problem as such. He argues that the influences of the response criteria are minimized by the design of the survey. That has, however, not been shown.

We do criticize the traditional methods used for scaling annoyance because it is implicitly postulated that the response criteria are invariant when proportion of persons is used as a measure of annoyance. We recommend methods that permit us to check the influence of the response criteria and, if needed, make the necessary corrections.

4. Dr. Rylander advocates that the reproducibility of his results is a measure of the value of the traditional survey and concludes that the problems raised by us are irrelevant in practice. We have to keep in mind that reproducibility is an elusive indicator because it is inversely related to the precision of the measurements. Thus a crude measurement technique will always result in a high probability of good reproducibility. It should be noted that the annoyance measures obtained in the traditional surveys that Dr. Rylander refers to are at their best rank orders of annoyance. It would be surprising if the rank orders could not be reproduced.

5. In the paper we show that the choice of the cut-off point is more or less critical depending on the distribution of responses over categories. The problem is illustrated by Dr. Rylander's own results that are presented in Tables 1 and 2 in his written comments. The good outcome of the rank orders is not a strong argument for the traditional survey, especially when Table 2 is consulted. There all persons, except for a few, are located above both the cut-off points he compares. In my opinion this result can have implications for Dr. Rylander's notion of a frequency maximum of aircraft flyovers as presented in his paper at this conference.

6. Dr. Rylander argues that the question of annoyance used by us is too general to have any reference to the noise exposure situation of the individual. Of course, there may be differences in the interpretation of slightly different questions, but I can hardly believe that the responses to the question on "annoyance to aircraft noise in general" are not at all related to the experiences of the aircraft noise exposures.

Regardless of this strange dispute on the phrasing of questions, Dr. Rylander's comments are irrelevant for the principles of measurement raised by us. It is up to him to show that "his" question is not influenced by response criteria variation. The absence of calibrated measures has many times led to invalid conclusions from results, e.g., in environmental toxicology. The need for calibration is the same in behavioral epidemiology.

7. Dr. Rylander's argument that only the highest degree of annoyance is well correlated to the exposure level does not go along with his earlier statement that the rank order of annoyance in Tables 1 and 2 are the same, independent of cut-off points. I also dislike the practice of selecting parts of the collected data in order to verify hypotheses about dose-response relationships. The aim of annoyance measurements must be to establish a scale of the annoyance felt by a population and then all the relevant data must be considered.

8. Dr. Rylander's comments on the calibration procedure are confusing. He says that the reference anchors must be experienced in the same way by all persons. If that were the case, there would be no need for calibration. In fact most comments made by Dr. Rylander strengthen our arguments for calibration procedures and improvements of the methods. Why we need calibration and what calibration does to the data are explained in the paper. For further information I refer to textbooks on theory of measurement.

9. Dr. Rylander has doubts about the validity of the improved method and concludes that our ideas are speculative. By definition the improved measurement procedure must be at least as valid as the traditional method, because the same basic data are used. What is added by the improvements is precision of measurement, provided the less restricting assumptions accompanied by the improvements are correct. The assumptions can and must be checked in every case, regardless of method used, whenever soft data are the basis for dose-response function.

10. I now realize that it will take time to introduce Thurstonian scaling methods as well as calibration procedures into applied research on annoyance. It is interesting to note that Thurstone presented his scaling methods as long ago as 1927. Since the late 50's, when the computer made the methods practical, the methods have been a valuable tool for quantifying psychological variables in the laboratory. It is my hope that also the investigators in the field will find the methods useful and also realize the need for calibration procedures and a well founded measurement theory. This is particularly important for investigators concerned with soft data such as are involved when gauging population annoyance.

THE ENVIRONMENT AND THE PROTECTION OF HUMAN HEALTH

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ABSTRACT

The study of the effects on human health of environmental agents derives its importance because of the opportunity it affords for prevention of disease and disability. Environmental health research provides the knowledge base for governmental decisions aimed at avoidance of undesirable or hazardous exposures. The list of chemical and physical substances treated in this manner is a very large one extending from air and water pollutants to therapeutic drugs.

The case for this activity is a compelling one when considering the opportunity afforded for betterment of health and the magnitude and far-reaching nature of the decisions which are based on this body of science. Yet, the body of knowledge available for decision-making is poor - both in quality and quantity and does not correspond to the capacity of science.

This paper discusses some of the characteristics of this area of scientific investigation and which sets it apart from others. It examines the consequences of lack of adequate information for decision-making. Finally, it makes a number of recommendations for the improvement of the scientific fabric for regulation.

1. Introduction

The fundamental motivation behind the study of the effects on human health of environmental agents is the potential opportunity for prevention of disease and disability. Environmental health research provides the base of knowledge and understanding fundamental to decisions (generally, government decisions) and standards aimed at avoidance of undesirable or hazardous exposures. Very large numbers of chemical and physical environmental substances are treated in this manner. Government decisions aimed at protection of health are made for both products and by-products of man's endeavors, including pesticides, ionizing radiation, air and water pollutants, food additives, etc. Although not always thought of as "environmental" agents, therapeutic drugs do, in fact, comprise a portion of man's chemical environment, present some of the same challenges of scientific understanding, and are treated similarly as far as patterns of research and methods of control are concerned.

It is interesting to note that, in the United States (and not uniquely so), most of the environmental legislation and environmental activity is performed in order to protect human health. The importance of an adequate base of scientific knowledge of the health effects of environmental agents is deserving of great attention. The extent to which the opportunity for prevention of environmentally-caused diseases is taken rests squarely upon the scientific fabric available for government decisions and upon the ways in which this base of scientific information is used in decision-making. Yet, to an unhappy extent, from a governmental point of view, the quality and quantity of the knowledge base for decisions is less than this subject deserves and less than science is capable of offering.

To a great extent our ability to understand the biological effects of chemical and physical substances such as pesticides, food additives and air pollutants has not kept pace with our technological ability to develop and use new substances. While some environmental agents seem to be clear causes of ill health, we must readily admit that detailed and systematic knowledge in this area lags far behind the levels of quantification and reliability accessible to contemporary science.

In 1970, the President's Science Adviser commissioned a broad review of chemical substances and their relationship to human health. The report of this review was published and released by the Science Adviser earlier this year. ^{1/} The review was intended to be a broad, yet extensive one covering several aspects of this complex area -- economics, legal questions and administrative procedures. The report reflects many of these studies and analyses. A large amount of attention was given to the subject of the base of scientific knowledge available for decisions.

The case for assuring an adequate knowledge base is a compelling one and the growing breadth of governmental decision processes attests to the importance of the research activity. The opportunity for prevention is particularly large and attractive.

In the United States, the crude death rate in 1900 was 17.2 per 1000 population. This rate fell fairly consistently through the first half of the twentieth century and by 1960 was 9.5 per 1000. (Figure 1). Between 1900 and 1960, large relative declines in mortality took place during infancy and childhood. In absolute terms, however, the declines in mortality at older ages were also substantial. Various deviations from this trend can be traced to epidemics of infectious disease which occurred from time to time before the 1940's.

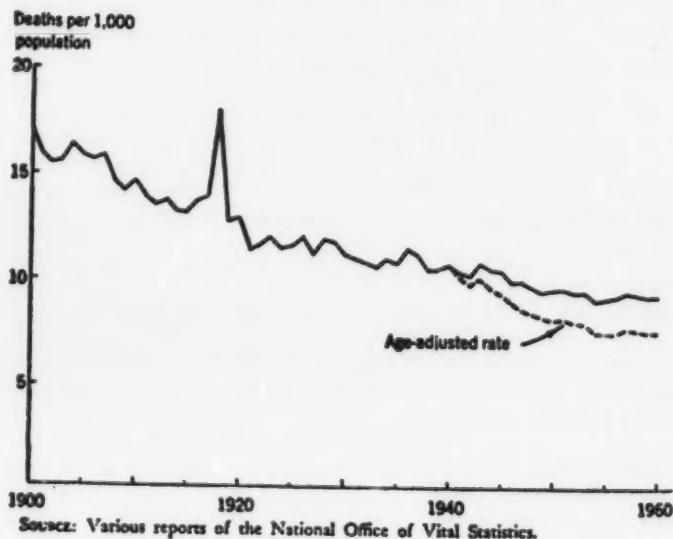


Figure 1 Crude Death Rates in 1900-1960 per 1000 Population in the United States.

It is important to examine the changes that have taken place in the rank ordering of causes of death by disease category. Notable has been the relative decline in importance of infectious diseases as compared to chronic degenerative diseases (cancer, diseases of the heart, arteriosclerosis, cirrhosis). (Figure 2). In 1900, diseases of the heart caused eight percent of the deaths in the United States and cancer caused less than four percent. By 1960, influenza and pneumonia were the only infectious diseases ranking in the top ten causes of death. (Together, these amounted to less than four percent in 1969.). At the same time

by 1960 diseases of the heart were responsible for 38 percent of all deaths and cancer for over 15 percent. Most important, these increases were substantially greater than could be accounted for by the decreases in deaths from infectious diseases and the increased portion of the population reaching advanced age. Thus, while cancer, for example, has "taken the place" of other causes of death, the increased age and size of the population does not entirely explain the increase in cancer deaths since 1900. 2/ The environmental contribution to human cancer in general is believed to be possibly quite large. 3/

It is interesting to note that in the United States, the long-term fall in overall death rates which characterized the first half of the twentieth century was interrupted in the decade of the 1950's by a flattening off. 4/ For males, the shape of the curve for mortality actually changed sign during the 1960's and passed from negative through zero to positive. The "excess" mortality (excess over what would have been expected from previously prevailing trends) was found to have been contributed principally by eight causal categories of which bronchopulmonary diseases accounted for over 50 percent. Figure 3 illustrates the major causes of death which were responsible for "excess" mortality in 1967 compared with 1960. The apparent influence of environmental factors (in a broad sense) on these extra deaths -- notably cigarette smoking along with other forms of air pollution and alcohol -- is very prominent. 1/, 4/

Finally, a striking series of observations of the past few years implicating environmental factors in the causation of disease has come from the series of migratory studies. 5/ In these studies, persons who migrate from one area of the world to take up residence in another appear to adopt the patterns of incidence of disease (notably chronic degenerative diseases) and causes of mortality of their new hosts in place of those characteristic of their former residence. Again, the implication that it is "something" in the environment which has led to the observed altered disease and mortality patterns is a very strong one indeed.

In spite of this strong, compelling case, in spite of the evident opportunity for a preventive endeavor, the storehouse of scientific information available for judgments and decisions concerning environmental health remains remarkably poorly stocked. The challenge of this task of research has not been taken up to any extent proportional to the importance of the issue nor commensurate with the capacity for scientific investigation. This marked disparity between the potential for scientific understanding and the dedication which this subject has so far attracted prompted one of the speakers at a forum on the Health Effects of Air Pollutants at the U.S. National Academy of Sciences to remark recently:

"We [scientists] owe someone an apology. How is it we could arrive at this point with so little understanding?" 6/

Figure 2: Leading Causes of Death by Disease Category in the United States.

Leading causes of death in the U.S. 1900 and 1960

Rank	Cause of death	Deaths per 100,000 pop.	Percent of all deaths
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1900

	(All Causes)	(1,719)	(100)
1	Pneumonia and influenza	202.2	11.8
2	Tuberculosis (all forms)	194.4	11.3
3	Gastritis, etc.	142.7	8.3
4	Diseases of the heart	137.4	8.0
5	Vascular lesions affecting the CNS	106.9	6.2
6	Chronic nephritis	81.0	4.7
7	All accidents*	72.3	4.2
8	Malignant neoplasms (cancer)	64.0	3.7
9	Certain diseases of early infancy	62.6	3.6
10	Diphtheria	40.3	2.3

(TOTAL)

(64%)

*Violence would add 1.4%; horse, vehicle and railroad accidents provide 0.8%.

1960

	(All causes)	(946)	(100)
1	Diseases of the heart	366.4	38.7
2	Malignant neoplasms (cancer)	147.4	15.6
3	Vascular lesions affecting the CNS	107.3	11.3
4	All accidents*	51.9	5.5
5	Certain diseases of early infancy	37.0	3.9
6	Pneumonia and influenza	36.0	3.5
7	General arteriosclerosis	20.3	2.1
8	Diabetes mellitus	17.1	1.8
9	Congenital malformations	12.0	1.3
10	Cirrhosis of the liver	11.2	1.2

(TOTAL)

(85%)

*Violence would add 1.5%; motor vehicle accidents provide 2.3%; railroad accidents provide less than 0.1%.

Figure 3 Major Causes of Death in 1967 Compared to 1960 in the United States.

Principal contributors to rise in mortality in 1967 compared to 1960 for white males. Diseases and conditions shown are those for which the number of extra deaths comprise more than 10 per cent of the total deaths from that cause.

<u>Cause of Death</u>	<u>Percentage Increase in Deaths 1967 versus 1960</u>
Carcinoma of the lung	22.9
Carcinoma, other, unspecified	14.2
Circulatory, other	17.0
Bronchitis	39.3
Bronchopneumonia, other	39.4
Cirrhosis	15.3
Motor vehicle accidents	4.6
Homicide	30.1

2. What Characterizes Present Knowledge for Environmental Health Decision-Making?

It seems useful to review some of the important characteristics which mark this area of science and scientific investigation. We have already noted that the totality of the investment in this field has been less than its importance would dictate and that its fruits have been accordingly scarce. As a reflection, several environmental standards (such as air quality and emission standards) have been based on relatively little scientific information.

The science of environmental health has at times been described as a frontier science. This title has been used to point up the frequency with which the results of preliminary scientific investigations have been taken directly from the laboratory and reflected in judgments and decisions regarding the environment. This process necessarily avoids (or evades) the avenues of interpretation of experimental results by the peers of the investigator, publication in scientific journals, confirmation through further experimentation and, therefore, the several means for maturation of investigative findings traditional to most of science. The consequences of preliminary, frontier, scientific evidence in decision-making for environmental health may, in the long run, be very serious and may not necessarily guarantee betterment of health.

A measurable amount of the scientific investigation in behalf of

environmental health has been of a low order of sophistication. The term, testing, has been used at times to characterize some of the investigation -- implying a process of accumulation of relatively gross observations reflective not of a particular hypothesis or matter of scientific insight but done more or less at random according to the spirit, the more data the better. 7/ This phenomenon has come about in part because of certain government policies which have encouraged such investigations. They may be laid in part, also, to the fact that this area of science has not always engaged the best professional and scientific minds.

Much of the scientific investigation for environmental health is performed only with great difficulty (still further limiting the number of willing and able investigators). Studies involving human subjects, for example, clearly essential for certain kinds of insight, are extraordinarily time consuming, are difficult logistically, and generally produce statistical associations rather than establish cause and effect relationships. Similarly, some investigations are aimed at an understanding of the low-dose and of dose-response relationship. These investigations, by definition, deal with low-probability events and therefore require very large experimental samples in order to assure statistical validity.

Finally, some mention should be made of the difficulties in matching the products of scientific research to the public expectations and to the requirements reflected in various legal instruments. For example, the establishment of environmental standards implies in many cases the identification of effective thresholds of effects. Major problems arise when multiple biological effects occur, when several organ systems are involved, and when effective thresholds cannot be established (or, in fact, do not exist). Further, the establishment of relationships between hazardous exposures and human subjects implies detailed or, at least, statistical knowledge of biological variability and knowledge as to how that variability is altered by diseases to give a pattern of known susceptibilities. This complex question of identification of susceptible members of the population and appreciation of susceptibility in reasonably detailed biological terms is one to which some discussion has been devoted recently although there remain large numbers of unanswered questions. 8/ Again, the degree of biological understanding presently available is far less than is implied by the present-day political and legal instruments. The science and its interpretation are generally found to be much more complex than is implied by most legal instruments and standard-setting procedures.

3. Consequences of an Inadequate Knowledge Case

The first and foremost consequence of an inadequate fund of scientific information concerning environmental health is missed opportunities for prevention of ill health. This, of course, is a serious con-

sequence since protection of human health is the rationale for environmental control and regulation. Thus, exposures to methyl mercury might have been avoided if the process of microbiological methylation of mercury had been recognized and if the unusual biological properties of alkyl mercury had been appreciated. Similarly, several years' exposures of occupational groups to radon-filled atmospheres in uranium mines and to coal dust occurred before the biological implications of these exposures were appreciated.

A second consequence is that of inappropriate decisions which are occasionally offered in the place of incomplete information. This is often an unfortunate consequence regardless of how well-intentioned the decisions may have been. Environmental decisions characteristically imply large expenditures of money and have far-reaching impacts (as, of course, they are designed to do). Because they provoke large rearrangements in our lives, however, they require and deserve the best possible foundation of information.

Decisions made in behalf of environmental integrity or improvement are typically definitive choices, or at least they are often perceived as such by lawmakers and by members of the public. Accordingly, once a decision has been taken, further research is often discouraged or suspended. There are, for example, few continuing efforts to determine the human health effects of DDT. Clearly, therefore, if decisions and rational actions are to be founded in scientific truth, we are at some peril if actions are taken on half-way knowledge and there is no promise of better information and possibly later confirmation or revision.

A striking (yet not well recognized) consequence of inadequate knowledge in recent years has been the result of trading inadvertently one environmental hazard for another. The removal of tripolyphosphate from among the ingredients of washing detergents produced the unexpected and unfortunate consequence of compromising the flame-proofing properties of chemicals added to clothing materials. Polychlorinated biphenyls, chosen as fluids for heat exchangers specifically because of their high level of stability at high temperatures, underwent certain restrictions. These restrictions may lead to an increase in the number of accidental industrial fires. More recently, the election of catalytic exhaust devices on automobiles in order to reduce certain automotive emissions may lead to an unexpected increase in the outpouring of other substances (sulfates and sulfuric acid mists) whose implications for human health are expected to be important.

Finally, and perhaps most important, the lack of sound scientific data for decision-making in the environment typically leads the political process to be unusually conservative (in the direction of protection of health). The consequent balancing of considerations and judgments becomes almost more difficult or impossible in the face of an implied threat than in the face of a recognized and documented hazard.

It is with these considerations in mind that the President's Science Advisory Committee urged that:

"Where knowledge is so inadequate as to make the reality of a possible threat quite tenuous, the proper response is to seek more knowledge, not either to take drastic action or to do nothing." 1/

4. What is Needed

The task of gaining new knowledge for this area of public decisions is an enormous one to the extent that it has appeared overwhelming to some who are charged with establishing its priorities. Yet, however acutely that message is felt within the scientific community, it is not well appreciated by others. There is need for biological insight across a broad front for environmental substances. At least as important, however, is a strong need for an increase in the level of sophistication of the research performed. Much decision-making reflects the results of gross "testing" -- the fulfillment of "standard" or "established" procedures. By contrast, there is an impelling need to insert a new but clearly attainable degree of sophistication into the research performed for the environment and health. Investigations should reflect specific hypotheses and scientific insight and should aim at uncovering an understanding of biological mechanisms of environmentally-related diseases.

In the United States we have come to recognize the need for more new knowledge in the areas intermediate between basic biology on the one hand and research closely related to immediate regulatory problems on the other. This has dictated a policy of encouraging a variety of various institutions serving this area.

Human studies represent a separate challenge. Clearly, some types of information can only be gathered from human experience. Commitments to epidemiological research and other types of human investigations imply and require long-term dedication and continuity.

There is a strong need to engage in forecasting -- to look around the corner in order to anticipate problem areas and to set priorities for research. This subject has attracted much attention in recent years. However, there are as yet relatively few tangible results. Attention has recently been afforded a methodology to forecast new and forthcoming technological events, new materials, and new uses of materials, specifically in order to point directions for biological research. In addition, a project in its early stages in the National Institutes of Health aims at ranking chemical substances as potential hazards according to the amounts produced, patterns of use, and distribution and modes of disposal.

Finally, there is a clear need for a reconciliation between the

traditional scientific conservativeness and deliberateness in judgment and the need for interpretation of scientific information for public and social understanding. The public is bound to pose broad questions on what the scientific data mean for the public's health. Since there is a technical or scientific base for their questions, they deserve a sound scientific judgment. Clearly, a regulatory agency of government needs to react appropriately and soon in the face of new scientific findings, clearly implicating a hazard to human health. Few would argue with the judgments taken in behalf of thalidomide. Yet, there is perhaps an equally strong need to preserve the deliberate quality of review and interpretation in order to assure the quality of information. Because of the scientific and technical nature of these decisions, scientists must be engaged actively in the process of interpretation.

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DISCUSSION

GOLDSMITH (U.S.A.)

Dr. Burger has raised a set of questions about the store house of information needed for health protection decisions. But to press the analogy further we must obtain a better inventory of what the store house contains and what of value is there. Prof. Holland for example noted the value of vital statistics. But now we have permitted the already available health statistical resources to be of less value than it should be by not using modern data handling methods. The result is that we lack the ability to detect and respond to trends and gradients in morbidity and mortality which may be affected by environmental exposure.

I note comments in your paper on the poor quality and inadequacy of environmental health research. I feel obliged to respond that not all the faults are those of environmental health scientists whose work has had such an unstable level and pattern of support. For example work of the quality and scope of that, for example, of Dr. Waller, cannot be undertaken. In 1967 the U.S. Department of Commerce's Technical Advisory Committee Panel on the Electrically Powered Automobile noted the difficulty of sustaining an adequate programme of research on health effects of motor vehicle exhaust with the pattern of research support suitable for short-term problems. Yet the situation today is as discouraging as it was then. The faults lie to some extent with the general scientific community which has been satisfied with short-term research support, with an inadequately responsive research policy, and to a small extent only with the environmental health scientists. We need and deserve a programme of stable, adequately supported, well planned research among countries and including intergovernmental agencies as well.

BURGER (U.S.A.)

The purpose of my paper was mainly to offer some observations on the state of affairs relating to Governmental decisions for the environment and on the knowledge available for those decisions. Your comment about the importance of continuity of research in this area is, of course, absolutely correct. It is one to which I can only subscribe enthusiastically and, in fact, I alluded to it myself in my presentation. I applaud also your own efforts to learn how to glean further clues relating to environment and health by better exploiting data which already exist.

However, I must insist that what I observe as a mismatch of the capacity of science and decisions for the environment is symptomatic of additional factors and will persist unless some fundamental questions are settled. A major problem seems to be

one of having permitted health to act as a surrogate for other desirable features in the environment - thus forcing political decision-makers at times to search desperately among the health sciences for arguments for action. A second is the short period of time considered by many as permitted for coming to decisions. This factor alone discourages long-term investments in background research. I would like to disabuse this audience of the idea that decisions must be made in every case rather than waiting for adequate information. Here, I quoted from the report of the PSAC Panel on Chemicals and Health on this very point.

A major problem which has inhibited adequate long-term investments in environmental health research and, in some cases, appropriate sophistication of research, has been a relative lack of understanding or concern among members of the environmental community for the importance of good scientific endeavor and information. This has been a serious factor from which many other problems seem to have been derived.

BERLIN (Sweden)

I appreciate your pointing out that there is a lack of knowledge about important areas in connection with environmental control. What is your advice to the administration? Should we not allow further change of our environment until enough knowledge is obtained or should we avoid interfering in the change of our environment until enough knowledge is present?

BURGER (U.S.A.)

I cannot, of course, sustain an argument which says that no action towards betterment of the environment should be taken until we are fully equipped with all of the information. However, I do join many others in being very uncomfortable at times over very large decisions taken on the basis of almost no information. By the same token, it is not true, I believe, that a quest for a decision must inevitably and immediately be met by a decision to act. A decision at times to temporize while awaiting additional information may or will usually serve the public's best interest.

WASSERMANN (Israel)

Today's sessions are encompassed between the doubts of Dr. Peterson and Dr. Burger with regard to the concern for the validity of research data before taking a decision.

It is rather necessary to consider some valuable epidemiological resources which are not enough used at present. I refer pro domo as an occupational health professional to the need for giving more attention to the amount of scientific investigation which could be carried out and obtained from the investigation and data in the industrial plants.

BURGER (U.S.A.)

I can only concur with Dr. Wassermann's recommendation in favor of exploitation of experience from the occupational environment in considering the general community environment. As some other participants in this symposium have indicated, information concerning occupational and industrial health experience is not always available in the published literature. Neither is this experience always systematically perused when available when considering prospective human epidemiological studies.

RECHT (C.E.C.)

The problems raised by Dr. Burger are extremely important and point clearly to the relationships between the scientific world, public opinion and the authorities responsible for decision making.

Certainly, with the use of the mass media and the interest shown by public opinion in environmental problems means that public opinion has easier access to scientific information, but does not mean that these data are easier to interpret as a result. Quite the opposite, in fact; in the United States a few years ago we had the example of the nuclear controversy, when the simple adoption by a few scientists of a position different from that of the scientific majority meant that doubts were raised as to the whole subject of nuclear expansion and that biased and even false interpretations of scientific data were taken as a basis for emotional attitudes.

A closer relationship must thus be established between science and politics, and scientists must assess the possible psychological effects of information which they impart sometimes incautiously and often in all good faith. It is also certain that this Symposium will fulfil the need for arriving at the widest possible consensus of scientific opinion on a number of methods, concepts and doctrines on which any real initiatives to reduce environmental pollution and annoyances will be based.

BURGER (U.S.A.)

I spoke to Dr. Recht's point concerning the relationship between scientists and public information. In my experience, it is an exceedingly important consideration in practice and has, at times, gone far toward influencing individual decisions. Responsibilities for active yet appropriate participation appear to lie with several parties to this question - the scientist, the press, and government agencies. (For a fuller discussion, I would refer the reader to the report of the Panel on Chemicals & Health of the President's Science Advisory Committee referred to in my talk).

POPULATIONSENTERSUCHUNGEN

POPULATION STUDIES

ETUDES SUR LA POPULATION

STUDI SULLA POPOLAZIONE

BEVOLKINGSSTUDIES

(Continued)

Vorsitzender - Chairman - Président - President - Voorzitter

M. COLOMBINI (Italia)

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THE STRENGTHS AND WEAKNESSES OF POPULATION STUDIES IN ASSESSING ENVIRONMENTAL HEALTH EFFECTS

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ABSTRACT

The basic purpose of the environmental regulatory process and the impact of the political and social framework on the design of health effects studies is briefly reviewed. The strengths and weaknesses of clinical and toxicological studies are outlined, and a more detailed exposition for population studies is presented. The problems of response indicators, exposure quantification, causality of association, combined pollutant effects, and the threshold concept are discussed. Four areas for further development in population studies are presented.

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It is often both helpful and revealing to step back and attempt to achieve a fresh perspective by identifying the primary purposes of work in the environmental health sciences. This is particularly true for those whose work is related in the last analysis to environmental regulatory decision-making. The primary purpose of the complex network of legislation, as well as federal and state regulations on environmental protection, in the United States and in many other nations has been and continues to be the protection of public health. Initial programs to improve public sanitation, when coupled with the advances in acute infectious disease control over the past 75 years, have significantly lengthened the life expectancy of the average individual in many nations. As an increasing percentage of the population has reached the seventh decade and beyond, the possibilities of developing chronic degenerative diseases has increased. These chronic diseases, most frequently seen in the older age groups, may be caused or exacerbated by chronic exposures to relatively low levels of many different environmental contaminants. In the past decade, regulatory decision-making has become much more complex and the legislative framework much more extensive. The primary objective, however, remains the protection of public health. Recent legislative initiatives have introduced the broader concepts of protection of general welfare, consideration of ecological impact, and improvement in the quality of life as secondary goals for environmental regulations. The role of economic and social factors in regulatory decision-making raises heated controversy amongst both scientists and administrative/political decision makers. In some activities in the U.S.A., e.g., in determination of primary ambient air quality standards, regulatory decision-making is constrained by law to consider only the protection of public health. In other areas, not only is public health a major factor, but ecological, economic and social factors play a significant role in the ultimate decision-making as well.

The central issue addressed in this paper is how health science data, particularly population studies, can be most effectively used in regulatory decision-making. In this context, all the steps in decision making must be considered, from problem identification and assessment to alternative control strategies, implementation and enforcement of a control/action program, and ultimately to an assessment of the efficacy of the action program. How this can be done depends, to a large extent, on what societal goals are chosen by political decision makers, as they construct the framework in which the issues will be evaluated. That is, specifically, the level of environmental protection to be achieved by any regulatory action must be predicated on a clearly stated choice between two different approaches. These designated levels of protection reflect two philosophical viewpoints. The first is the classical zero tolerance or no risk approach, which states basically that when dealing with any toxic substance in the environment, no health risk is acceptable. Therefore, when zero tolerance is the basic premise, it leads to zero exposure programs. This approach has been adopted by the U.S. Congress for dealing with carcinogenic materials in foods and drugs under the Delaney Clause. A slightly less stringent corollary is the threshold or no-permissible-adverse-health-effects approach. This concept is the basis

for the Clean Air Act provisions establishing primary ambient air quality standards. In this case, exposure limits are set at levels where no adverse health effect can be measured.

More recently another conceptual framework has been advanced—that of socially-acceptable risk. This approach has been used to determine some industrial exposure standards and most recently was used as the basis for the U.S. Environmental Protection Agency's (EPA's) proposed benzidine effluent guideline. There are many difficult questions inherent in applying this approach, both from statistical/mathematical point of view and from moral/ethical considerations. This concept requires two decisions. First, one must make certain assumptions as he extrapolates from known dose/response data to the low dose/low risk portion of the dose/response curve. There are many models that have been proposed for this extrapolation. Two of the more commonly employed are the Mantel-Bryant probit model (1) and the linear "one hit" model (2). Thus these abstract models have dollar and cents reality when used in the decision-making process of a regulatory agency. The plenary discussion will develop in more detail some of the trade-offs involved in balancing health effects with economic, social and energy related factors as they relate to the assessment of a socially-acceptable risk and to a determination of regulatory policy.

What tools and mechanisms are available to generate the health-related data necessary to formulate rational, efficient and effective environmental regulatory control strategies?

It is helpful to view environmental regulations as a four-step process (Fig. 1). [3]

SIMPLIFIED SCHEMATIC OF THE ENVIRONMENTAL CONTROL PROCESS

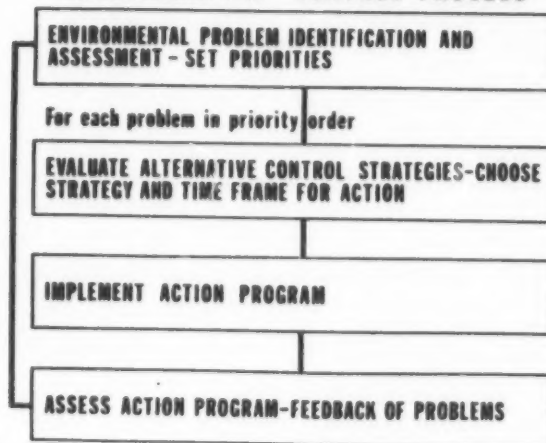


Fig. 1. Simplified schematic of the environmental control process.

1. Problem identification and assessment.
2. Developing alternative control strategies.
3. Implementation and enforcement of an action program.
4. Action program assessment.

In all steps except implementation and enforcement, it is crucial to have an adequate scientific data base as the foundation for the political-regulatory decision process. Problem identification often requires much less data than that required to develop alternative strategies and select the most appropriate regulatory action. One cannot assess the impact of any action program unless he has adequate base line data to assess the situation prior to the initiation of that program, plus well-designed follow-up studies to assess the "benefit" of the program.

Health scientists have three major weapons in their arsenal, clinical studies, toxicology and epidemiology or population studies (Fig. 2).

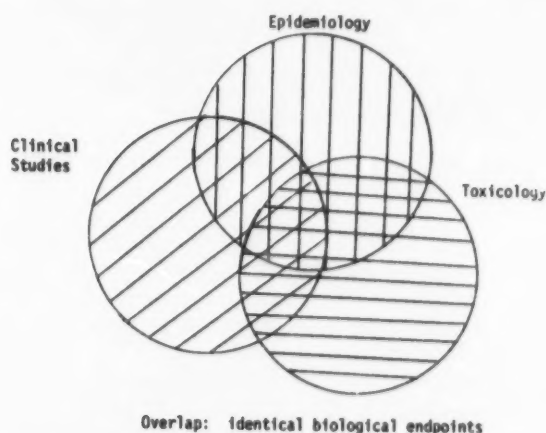


Fig. 2. Methods to demonstrate biological response to pollutants.

Clinical research studies can be used to gather human data on either normal or diseased individuals regarding the absorption, metabolism, and excretion of pollutants. This is particularly useful in the evaluation and in-depth analysis of humans accidentally exposed to high levels of pollutants where new parameters of exposure and indicators of response can be identified. The advantages of clinical studies are: (a) that there is a controlled or at least relatively accurately-quantifiable exposure to a pollutant. Thus in experimental protocol studies one can obtain improved dose measurements; (b) often one can use each person as his own internal control (before, during and after exposure), thus effectively controlling many covariates; (c) vulnerable subjects may be

included by design to increase the sensitivity for low-dose responses; (d) cause-effect relationships are more easily deciphered; (e) cross-species extrapolation of the results is not necessary. This maximizes the usefulness of these data in setting health-related pollutant standards. There are three major limitations to clinical studies:

1. The exposure profile is artificial.
2. No long-term exposures are possible, so only acute effects can be determined.
3. There is a small but real hazard to the exposed subject.

Toxicological studies are a second tool, which use many response systems, including whole animal, tissue culture and biochemical systems. The advantages of toxicology studies are: (a) maximal dose-response data can be obtained, though this is often incomplete at the low dose portion of the curve; (b) data acquisition is relatively rapid; (c) cause-effect relationships are more easily established; (d) studies on the mechanism of response, such as pollutant absorption, distribution, metabolism and excretion, can be performed. However, toxicological studies often lack appropriate human disease models in laboratory animals, thus the effects of the controlled and well-characterized-pollutant exposure are evaluated in most cases only in healthy animals. This limits the sensitivity of this tool in evaluating subtle but possibly important changes in certain relatively common human disease states. Only recently has this tool been used to identify and evaluate delayed responses or chronic cumulative effects of exposure. It is also very difficult to duplicate in the laboratory the exact exposure profile for a given pollutant in a community. The generic problem of extrapolating data from laboratory animals to the human subject remains particularly difficult, especially when one is attempting to use this data to estimate a "threshold" level for adverse human response.

Epidemiology or population studies, the main focus of our considerations here today, offers certain unique advantages. It provides studies on the effects of pollution exposure on populations in real-life settings. Thus the exposure profile is natural, reflecting the real-world situation. There is no problem with extrapolation of the results from one species to another. This tool enables the environmental health scientist to study the most vulnerable population groups, not just the healthy population. It allows evaluation of the effects of current exposure levels, crucial for meaningful and timely regulatory decision-making, and of the effects of exposure to chronic low levels of various environmental pollutants.

There are certain key limitations to epidemiological studies, which must be kept in mind when assessing how most effectively to use population studies in regulatory decision-making. The precise quantification of the exposure profile for each individual is very difficult, if not impossible, to determine. A corollary of this problem is that often one cannot obtain any dose-response curves. Epidemiological studies by their very nature must deal with a multiplicity of covariates, often making isolation of the single variable under study virtually impossible.

Unless the pollutant under investigation in an epidemiological study has already been introduced into the environment for a long enough period of time to cause a measurable effect, such studies are often unrewarding and may lead to an incorrect epidemiological "clean bill of health" for a recently-introduced new chemical/pollutant. Thus in the study of new chemicals, epidemiology has limited usefulness and certainly is of little predictive value. Finally epidemiological studies are much less powerful tools than toxicological studies or clinical studies for establishing causality in the association of a given exposure and a measured effect.

How then can epidemiological studies be designed to maximize the strengths, minimize the weaknesses and thus make the study of maximal utility in regulatory decision-making?

First a more precise understanding of the spectrum of responses for exposures to any given pollutant must be developed. There are five basic levels of response to exposure of any given pollutant (Fig. 3). [4] At the lowest levels, affecting the largest population groups, exposure to a pollutant may increase the total body burden of the pol-

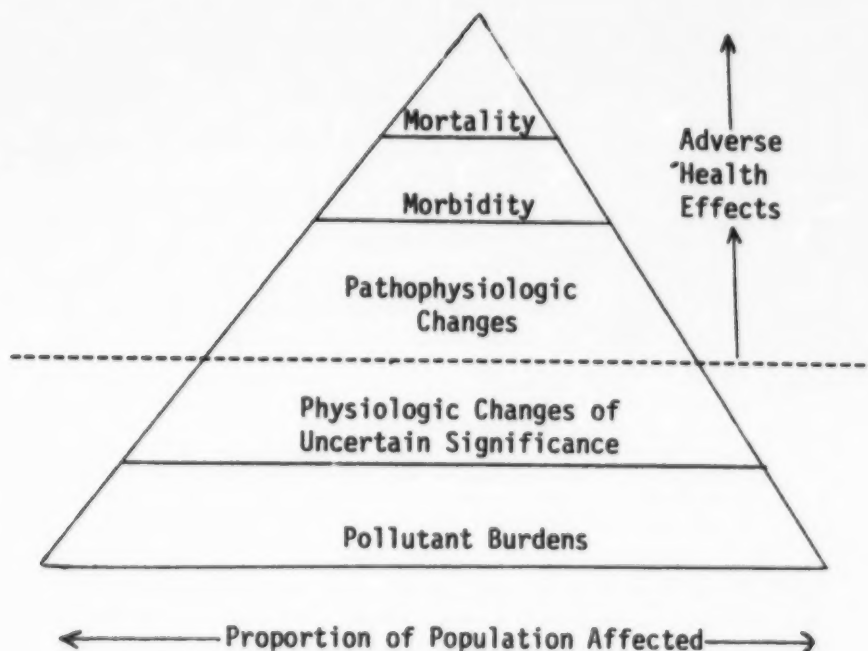


Fig. 3. Spectrum of biological response to pollutant exposure.

lutant, without any measurable effect on the health, metabolism, or physiology of the organism. Exposure to lead with increased body burden but blood lead levels of less than 25 $\mu\text{g}/100\text{ ml. blood}$ is an example of this "response" level. The next level would be exposures which lead to metabolic or physiological changes of unknown significance, such as the increased urinary excretion of delta- α -aminovaleric acid associated with blood lead levels of 40 $\mu\text{g}/100\text{ ml. blood}$. This blood lead level is not associated with significant organ dysfunction or any increase in acute or delayed morbidity. The third level is that exposure which causes a physiological or metabolic change that is clearly premonitory, such as exposures leading to decreased mucociliary clearance in the respiratory system or changes in pulmonary function tests. Next are exposures that elicit frank disease, such as initiating an acute asthmatic attack or causing an increase in acute lower respiratory tract infection. The final level is that which leads to death. With the multitude of covariates often associated with increased mortality, it is difficult to establish exposure to a given pollutant as the sole "cause" of the excess deaths. The role played by diet, aging, accidental injury, and individual variability in susceptibility must be considered.

In the vast majority of cases, one deals with a response continuum and rarely with a discontinuous, all or nothing event. The information gap between the level of pollutant body burden and that of overt disease state must be bridged before the role of pollutant exposure in total community morbidity can be precisely defined. The population studies are particularly effective in studying those groups most susceptible to the adverse effects of environmental factors, such as the very young and the aged, or to evaluate the effect of pollutant exposure on populations with specific diseases, such as asthma or chronic respiratory disease.

It is also of great value in assessing the effect of pollutant exposure during periods when an individual's susceptibility is temporarily impaired, as during pregnancy, the adolescent growth spurt or acute lower respiratory tract infection. [5] Populations in whom susceptibility is permanently altered, such as alpha-one antitrypsin deficiency states or abnormal hemoglobins, can also be studied.

Disease states are the end product of an intricate and complex causal web. [6] Each individual strand must be isolated and evaluated. But to understand fully the "gestalt" of environmental pollutant exposure, nutritional status, genetic composition and personal habits, the strands must be woven together again. Man's natural intuitive concepts of the nature of response may not be entirely accurate. For example, there is no reason why one could not postulate that exposure to an environmental pollutant could cause an increased severity of preexisting disease without increasing the overall incidence of that disease. In this case, classical incidence studies would miss the significant "health effect."

The horizons of the responses measured must be broadened. In a large number of the classical environmental pollution population studies, either death rate, pulmonary disease symptoms or cardiopulmonary symptoms have been chosen as the dominant or sole criteria for judging adverse health effects. These areas of response may well be the major patterns for exposure to the common airborne pollutants, but it is

essential that other parameters of adverse responses must be developed. Both more precise and sensitive biochemical and physiological indicators in many organ systems are required. Recent work with enzyme systems as response indicators or system dosimeters shows much early promise.

The interface of response and exposure presents its own difficulties in designing and conducting optimal epidemiological studies. One must be able to assess accurately the duration of exposure, the concentration of the pollutant(s) and the rates of change in levels of exposure. He should know the route of exposure, which is not as simple as it may appear, e.g., the possibility of swallowing inhaled fibers after they are cleared by mucociliary action in the respiratory tract. He must generate data on the uptake, metabolism, and excretion of the pollutant. It is important to be able to assess individual variability in response related to physiological variability, climate, occupational history, and psychosocial factors. This responsiveness is also tempered by tolerance and adaptation. The physical and chemical properties of a given pollutant also affect their potential to elicit an adverse effect. Thus the size, density, viscosity, volatility, solubility, chemical reactivity and electric charge of the pollutant must be quantitated as precisely as possible. The more data available about the photochemical and thermochemical transformations which a pollutant undergoes as it moves through the environment from source to receptor, the more precisely one can assess the toxic potential of any given pollutant.

The measurement of exposure is fraught with difficulties. [7] The population under study in the U.S.A. is highly mobile and often transient. Twenty percent of the U.S. population changes place of residence every year. On the average, 1/3 of the population of a U.S. community has lived there less than three years. The pollutant mix is also variable, changing with both time of day and season. For air pollutant exposures, the activity pattern of an individual during a "normal day" carries him through areas of potentially markedly differing pollutant mixes and concentrations. The duration of exposure in each area is different for different individuals. There are not enough different air quality monitoring sites in any one area to construct an exact exposure profile, even if all could agree on a reasonable activity pattern or patterns. In the U.S. Community Health and Environmental Surveillance Studies (CHES), each area selected for study must meet certain criteria, with no large point source of pollution, relatively simple flat topography and relatively complete census tract data available. Then a single monitoring station is constructed near the center of the area. However, for reasons of accessibility of building sites, often the sampling site is far to one side of the area. Recently, mobile samplers have been used to check the uniformity of pollution levels in the area. It is unclear what constitutes the most effective technique for dealing with data from an area in which the pollution levels are not uniform. The question of exposure profiles, cannot be resolved with the present data base, as many will leave the area for significant periods of time each day. This often causes exposure to very different pollutant levels in these other areas.

One way to avoid some of the problems with quantifying exposures is to develop personal exposure meters, analogous to the X-R film badge. EPA is supporting the development of a personal exposure meter for sulfates, and it would appear that the technology could be developed

for some other pollutants as well. Such devices would have certain very important benefits. They would permit validation testing of activity/exposure models for much larger populations than would wear the monitors. They would help determine the appropriate placement of stationary monitoring sites for larger scale studies of similar populations. They can help assess the health impact of differing pollutant exposure levels. However, they suffer from several drawbacks. The Heisenberg principle of uncertainty introduced by observation may play a role if behavior is modified by knowledge the individual is being monitored. Any study using such personal monitors would be expensive, limiting the sample size. It would require excellent participant cooperation. Reliability would have to be firmly established, and it would be difficult to use the data to establish a threshold or to construct an appropriate control strategy.

The alternative to expanded development of personal exposure meters is expanded use of stationary monitors. This generates data which can be applied to large numbers of individuals, if one assumes certain activity patterns. These data are necessary for accurate assessment of the effects of short-term exposures. Continuous monitoring equipment is also expensive and the complex technology is prone to breakdowns at the most inopportune times. Too often the monitoring data from these stations is disassociated in space and time from the measured health effects. Frequently disease incidence studies in metropolitan areas are correlated with exposure estimates based on data from one or at most a few stationary monitoring units. These data may not be representative of community-wide exposure. The derived exposure estimate may imply exposures higher than actually occurred. On the other hand, ascribing excess chronic disease to currently-measured levels of pollutants may underestimate the real long-term exposure, since air pollution levels in the late 1940's and 1950's were higher than in 1970-74. Perhaps the weakest link in our attempts to establish the exposure-response relationship is in obtaining an accurate quantitative estimate of exposure. To base regulatory decisions on very precise and extensive health response data, but relatively poor exposure data, can lead to gross errors in regulatory judgments.

Once statisticians have shown an association between an exposure and a response, how can one best evaluate whether or not there is a causal relationship as the basis for that association? Hill [8] has developed a set of criteria to judge whether or not an observed exposure-response relationship is causal. Although these criteria were developed as guidelines for occupational health studies, they can be adapted for application to general population studies. The major criteria are: (a) consistency of observation; (b) coherence of data; (c) plausibility of association, and; (d) strength of association.

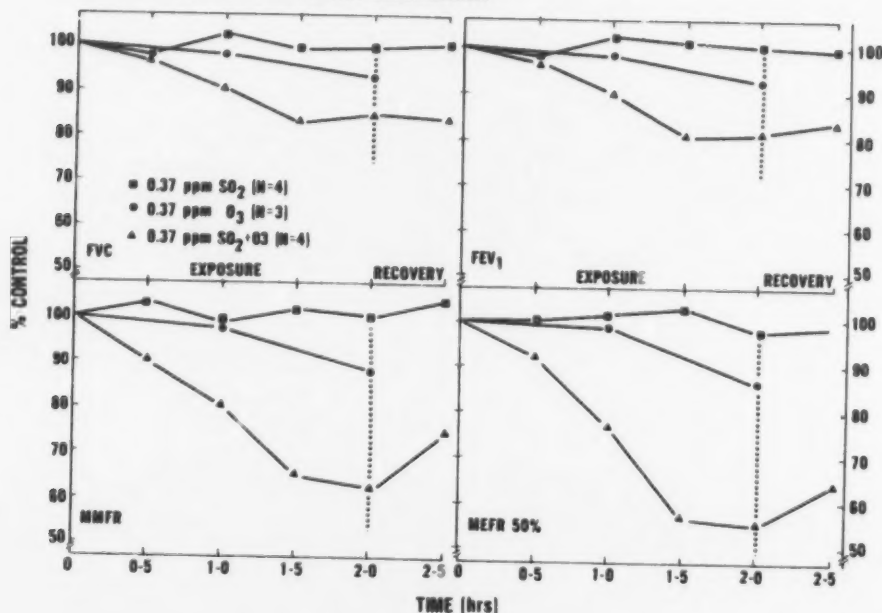
Other factors which can aid in the evaluation of the significance of exposure-response associations include: (a) the presence or absence of an exposure-response gradient. When there is a stepwise increase in the frequency or severity of the adverse health effect, this supports a causal relationship. Linear relationships over an exposure (dose) gradient are difficult to explain by the intervention of other variables. Such gradients are most easily created in experimental settings, but can be approached in population studies by investigating the relationship of response to exposure gradients across geographic areas, differences in

length of residence in high exposure areas, and migration gradients constructed from various combinations of childhood and adult exposures of the same individuals; (b) Intervention: The effect of societal programs designed to protect the public health from observed adverse health effects associated with exposure to a given pollutant can be helpful in establishing causal relationships. If, as desirable environmental ambient levels of the pollutant are achieved, the frequency/severity of adverse effects diminishes, there is a strong suggestion of causality. The high cost, both in the public and private sector, of many of the environmental regulatory programs warrants a vigorous national program of community health and environmental surveillance to evaluate with more precision the benefits of these abatement efforts; (c) Control of covariates: The causal nature of an exposure-response association is convincingly identified when, after the effects of known covariates are first displayed, increased disease risk within covariate classes can be clearly demonstrated in high exposure populations. For example, in any studies of chronic bronchitis prevalence, smokers and males show more disease than nonsmokers and females respectively. An air pollution-chronic bronchitis study should reveal the above smoking-sex differences in prevalence rates, thereby assuring readers that the study has internal consistency. If smoking and sex specific groups in high exposure neighborhoods have excess chronic bronchitis, the hypothesis that air pollution exposure causes excess chronic bronchitis is considerably more convincing than if the smoking-sex covariates were not analyzed. Most epidemiologic studies of air pollution require similar analysis of excess disease risk within covariate categories, with particular attention given to age, sex, smoking, socioeconomic level and duration of residence at current location. When covariates are systematically analyzed for relationships to the health indicator under study, residual excesses in disease frequency can be attributed to differences in pollution exposure with a reasonable degree of confidence.

Such population studies have been classically designed to hold constant all variables but the one under study, and this has been a powerful tool. Yet as one looks at more complex exposure profiles, with pollutants which could act in a synergistic, additive, or ameliorative manner, he must develop and employ more sophisticated multivariate analyses. He will require methodology to identify possible interactions of various pollutants. The relatively limited data base available in most cases makes it difficult to complete such an analysis. The data base must be expanded to include increased data on the combined effects of multiple pollutants. The physio-chemical interactions occurring among different pollutants in the environment often alter the biological activity of the pollutants, as well as modify the response in the exposed individual. A recent example of a study of combined synergistic effects was presented by Bates and Hazucha [9] in 1973. They stated "our most recent experiments have been concerned with an additional problem, namely a possible interaction between ozone and SO_2 . The episode of pollution in Rotterdam that occurred two years ago had several puzzling features. Although the ozone levels did not reach much beyond 0.2 ppm, and the SO_2 levels at the same time were about 0.2 ppm also, there was considerable morbidity, particularly amongst people bicycling in such an atmosphere. These levels of the individual constituents seemed to be too low to have caused the considerable symptoms which were reported. There is evidence that ozone and SO_2 together affect plants at lower concentrations than each would individually, and since now-

days ozone exposure and SO_2 exposures may be expected to occur together, it seemed most important to us to try and study the interaction of the two." This Figure (Fig. 4) [9] shows the effect on four measures of pulmonary function of 0.37 ppm of SO_2 and 0.37 ppm of ozone exposure independently, and then the enhancement of effects when both gases are present simultaneously. It is interesting to note that the effect of

THIS FIGURE SHOWS THE EFFECT ON FOUR MEASURES OF PULMONARY FUNCTION OF 0.37 PARTS PER MILLION OF SO_2 AND 0.37 PARTS PER MILLION OF OZONE INDEPENDENTLY, AND THEN THE ENHANCEMENT OF EFFECT WHEN BOTH GASES ARE PRESENT SIMULTANEOUSLY^a



^a BASED ON FIGURE 14, PAGE 534 OF U.S. CONGRESS DOCUMENT NO. 93-15

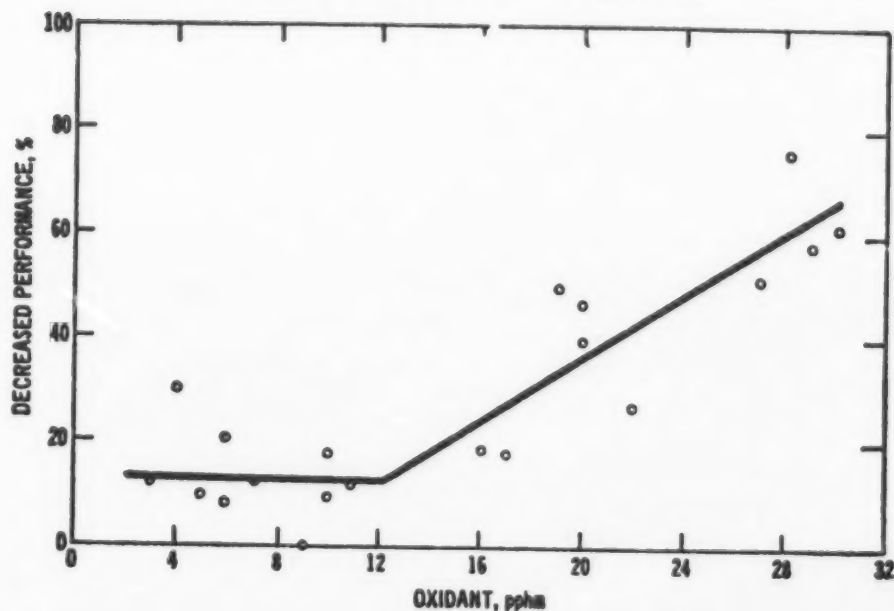
Fig. 4. Effect of SO_2 and ozone on pulmonary function.

the two gases administered simultaneously is greater than the sum of the effect of each individually, thus demonstrating a synergistic effect. Similar synergistic reactions may well explain many other episodes of pollution-related disease in Europe, Japan, and the U.S.A. Until population studies which can evaluate this possibility are conducted, it will continue to be difficult to select the most appropriate control level for each individual pollutant to ensure adequate protection of public health, while avoiding unnecessarily restrictive standards.

A final area of methodological concern is the use of the concept of "threshold" in epidemiological studies. A biological effect may not be observed until the exposure (dose) reaches a certain level. This "threshold" dose is defined as the minimum dose required to produce a

detectable effect. The nervous system has been cited as an example of an "all or none" or "threshold" biological system. However, it is now well established that, on a membrane level, much of the response in the nervous system is a continuum and is not "all or none." The concept of a threshold dose for a potentially harmful pollutant is important from both a practical and a theoretical viewpoint. It implies that there is a "safe" limit or standard which can be specified. However, as the indicators of response become more sensitive, the "threshold" may appear to decrease. For many pollutants, there may be no real "safe dose," [5] while for others existence of a "threshold" may reflect the development of tolerance to a particular pollutant. This adaptation to long-term, low-level exposure to a given adverse environment varies within a population and is determined by an individual's anatomic, physiologic, and biochemical characteristics [5]. Even if we set aside the consideration of the biological reality of the threshold concept, the statistical methods employed to approximate this level have their own limitations. The EPA National Environmental Research Center group has adapted from Quandt [10] an approach to estimate "threshold" by fitting the data to two best-fit lines, one with zero slope and one with a positive slope (Fig. 5) [11]. This "hockey stick" analysis then uses an iterative

STATISTICAL ASPECTS OF SURVEILLANCE



Per cent decreased performance *versus* oxidant level, with fitted "hockey stick" function.

Fig. 5. Statistical aspects of surveillance.

process to reach the least squares combination of the two lines and the point of inflection is then taken as the threshold. This has been used in setting the U.S. primary ambient air quality standards, and is particularly helpful if a series of studies generate similar "hockey stick" thresholds. However, the inflection point determination may not be unique and the analysis assumes that the positive slope response curve is linear. Also, the method is univariate and the only method for evaluation of multiple covariates is to assume their presence and add a statistical factor to account for their influence. Finally, the 95 percent confidence limit around the inflection point is often very broad and occasionally will encompass "zero" dose. Both the scientific community and the political decision-makers must continually reassess the validity of the assumption of applicability of a threshold concept to a given pollutant-response association. It may well turn out that some of these cases will require, in the future, assessment of the socially-acceptable risk rather than a set "no adverse effect" threshold.

As one looks to the future, what directions will be taken in population studies to maximize their usefulness in the area of environmental health regulation? It is absolutely necessary that more emphasis be placed on developing baseline data prior to the implementation of any environmental regulatory program. If this data is not obtained, neither the regulatory agencies nor the health scientist community will be able to assess adequately the effectiveness of regulatory programs or to convince the people and the political power structure that further programs are justified and worthwhile. A noteworthy example of this is the need to design and conduct such population studies before and after implementation of early projects under the \$18 billion waste water treatment plant construction grant program in the U.S.A.

A second area where increased future emphasis is indicated is in cooperative programs between population study designers and large health services delivery systems. There is a large potential data bank that can be gathered by organizations such as National Health Services in Europe and Canada and private Health Maintenance Organizations (HMO's) in the U.S. Some Union programs, including Rubber Worker's Union in the U.S., have made health data recording and long-term follow-up part of their contractual agreements with their employers. Environmental health scientists should develop similar data banks. This source has been much more effectively utilized by our colleagues in Europe and Canada, but EPA is presently evaluating a feasibility study on cooperative programs with several of the larger HMO's. The major challenge in this area is to develop an informational framework so that these long-range data sources can efficiently collect those data that will be most useful in the future.

Future epidemiological studies must also maximize the temporal and spatial concordance of exposure monitoring systems and health data. The coordination between the Regional Air Pollution System (RAPS) and the Community Health and Environmental Surveillance System (CHESS) in St. Louis is a step in this direction. But on a broader scale, measurement methodology and the health information should be standardized on a regional, national, and eventually international basis. This is particularly true as the distant effects, both regional and global, of air pollution are more fully understood.

I would like to place special emphasis on the need to generate health information from the population groups most affected by environmental pollution. The central-city inhabitants of many cities in the world are exposed to the highest levels of pollution, but these populations have been only infrequently included in epidemiological studies. It is obvious that studies in these areas are more expensive and far more difficult than studies dealing with suburban middle class, relatively well-educated population groups. Most of the classic subjective tools for collecting epidemiological data (diaries; long, complex data forms) are not effective in the inner city setting. Until the methodology to gather reliable epidemiological data from inner city populations is developed, a significant void in the data base required for optimal regulatory decision-making will exist. One avenue for improved data quality might be to increase reliance on objective tests, such as pulmonary function tests. The community experience of many university hospitals in center city areas is a potential source of expertise for optimizing the quality of subjective data from the diverse socioeconomic groups in these areas. The goals of such studies must be translated into clearly-perceived positive motivational factors, relevant for the individuals included in the study.

In summation, this paper has attempted to focus on some of the problems which face environmental health scientists and how population studies can be designed to maximize their usefulness and impact in the environmental regulatory decision-making process. It also suggests a few of the future paths which epidemiologists must take the lead in, as they strive to solve these methodological and informational problems. It will have served its purpose if it generates an exchange of ideas and perceptions on the issues raised or on the many issues not developed due to time constraints.

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DISCUSSION

ZIELHUIS (Netherlands)

Dr. Jackson distinguished between "public health" and "quality of life". However, health is a unified concept, although with different aspects:

- medical
- behavioural
- ecological

each of these studied by different disciplines.

There is no distinction between human health and quality of life, but only a sequence of priorities in regulatory measures of prevention.

The priority of prevention should not be determined by scientists (or physicians), but by the population itself. Very probably, the population has different priorities than, for

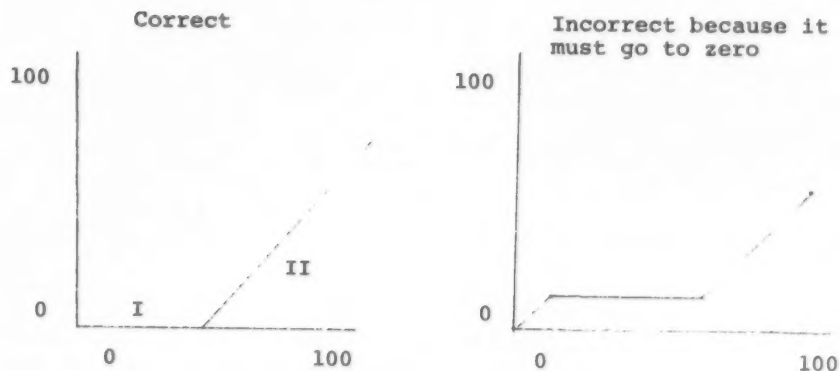
example, medical science. Priority setting is a political decision, and not the outcome of scientific discussion. Restricting health to medical aspects, already sets a priority, maybe not in concordance with priorities as set by the population.

JACKSON (U.S.A.)

Dr. Zielhuis raises some very important points. In my full text, the separation of "Classical" public health and the "quality of life" reflected the chronological sequence of the introduction of these concepts into the environmental protection legislative framework. In my own view, the concept of the quality of life is an integration of many factors, including the absence of disease, behavioral, socio-economic and ecological considerations. For a society to maximize this integral requires prioritization of these factors. These societal decisions are clearly beyond the sole province of the technique experts. I have tried to distinguish between the role of the scientific community and the political decision makers. The scientific community must identify and assess problem areas, generate the data, evaluate the data, and present an objective interpretation of the data to the political decision makers and the general public. This does not mean a scientist should not participate in public policy debate, but he must do some realizing he represents only a small segment of the population. For his position to be accepted by the general public, it must be made understandable and cogent to the decision makers and the public. It is clear the U.S. Congress reflected an inherent priority decision on the major role for protection of the population from disease, when it passed the Clean Air Act in 1970. This policy decision was taken by the elected representatives of the people, not by an elite corps of scientists. In the past four years, the areas of concern have been broadened, as detailed in the paper, reflecting a growing awareness that all factors must be considered in most decision making processes. However, the protection of the population's "medical health" remains a cornerstone of the environmental regulatory process, though it should no longer be considered the entire edifice, eliminating consideration of other important factors.

MAGE (Denmark)

Is not figure 5 faultily constructed? since the fitted functions must go to zero? decreased performance at zero pphm oxidant by definition. Is not the correct form, as dictated by this physical principle a horizontal line from the origin (0,0) followed by a linear section with a positive slope?



JACKSON (U.S.A.)

Dr. Mage has difficulty with the "hockey stick" analysis. In this, he has many companions. In the full text of my paper, many of the limitations of the threshold concept in general and the "hockey stick" analysis in particular are noted. However, when multiple studies generate many similar "hockey stick" thresholds, the value so determined can be useful in regulatory decision making. Figure 5 was chosen from a paper by Nelson et al to represent a graphic example of this technique. The "per cent decreased performance" refers to the performance of a high school cross-country running team, which ran the same course each week, timing each individual runner. Each team member's time was compared to his time from the previous week. The percentage of the team that ran slower on a given week was plotted against ambient oxidant level measured at the race course. Approximately 16% of the team ran slower than the previous week at all measured oxidant levels between 4 and 12 pphm. Only when oxidant level rose above 12 pphm did team performance show any additional decrement. Two points should be made. Although it is true there is no data on team performance in oxidant levels between zero and 4 pphm, the constancy of the 16% decreased performance, at decreasing oxidant levels from 12 to 4 pphm, would make a fall of the percentage decreased performance to zero at zero oxidant concentration quite unlikely. The myriad of other random causes for a team member running slower than the previous week other than oxidant levels makes this data intuitively plausible. If one subtracts the 16% as a baseline and plots change in decreased performance percentage above this baseline vs. oxidant level, one generates a "zero effect at zero level" curve that Dr. Mage prefers.

MOKEMATKENGUEMBA (Central African Republic)

Pollution is often said to be a problem peculiar to the industrialized countries. I should like to know whether:

1. Research or studies on pollution have been done in the developing countries in general and in Africa in particular? What were the findings obtained?
2. What forms of pollution are found in the developing countries?

JACKSON (U.S.A.)

I am particularly pleased that Dr. Mokematkenguemba raises the question of environmental issues in the developing nations. These nations have many significant environmental problems, though most are different than those facing the heavily industrialized nations. The major environmental problems in the developing nations have, in the past, been related to classical public health areas, particularly infectious diseases. My knowledge of the scientific literature from many of these areas, particularly Africa, is somewhat limited. There have been many important studies on the relation of water resource development projects and the wildfire spread of schistosomiasis, particularly in the Aswan Valley, West Africa and Tanzania. It is absolutely mandatory that new schistosomiasis control methods such as the slow-release organotin molluscicides, be thoroughly evaluated and vigorous control efforts must be coupled with any new water resource project in these areas. The ecological and human health disaster precipitated by the drought in the Sahelian area of West Africa has only recently been brought effectively to general public awareness in many of the industrialized nations. The U.S. Center for Disease Control has conducted epidemiological surveys in the Sahel, in conjunction with mobile health care delivery teams. They noted very high incidence figures for measles and tuberculosis especially in the children of those most severely affected - the nomadic herdsman. These illnesses are clearly related to nutritional deprivation and overcrowded, hastily constructed refugee camps. To meet the immediate human needs in this area, continued and expanded efforts from all concerned nations are required. I am not personally aware of studies in these areas on the more common industrial related pollutants.

In reply to the second part of your question, the problems of cross-frontier pollution or the distant effects of pollutants must receive more attention. The pollution of major water supplies, including the oceans, affects many nations, not only the industrialized nations. The evidence of particulate air pollution and DDT in Antarctica and the finding of fine particulate matter from the Sahara in the upper atmosphere over the Caribbean both serve to emphasize the "shrinking" nature of the

world. Bryson has hypothesized on the global effects of particulate air pollution. He implicates the increase in industrial-related air pollution over the past 25 years in the slight decrease in temperature noted in the polar regions over the same time span. This change in polar temperature, according to the hypothesis, caused a shift in the high pressure anticyclone and hence in the edge of the monsoon rain belts. This is advanced as at least a partial explanation for the drought in the Sahel. With the very real possibility of increased coal utilization in the near future it is vital to evaluate this hypothesis and test its validity, so as to either substantiate or disprove this possibility.

A particularly difficult area for the developing nations will be balancing the benefits of rapidly increasing industrial production essential for improving the material standard of living for the people of these nations, and the real "costs" of the pollution generated by such increased industrial activity. Perhaps some of the experience and mistakes of the industrialized nations can serve as useful data as each developing nation constructs its own priority system - in effect, its own optimizing of the "quality of life".

DESIGNING THE EXPOSURE/RESPONSE MATRIX IN ENVIRONMENTAL HEALTH STUDIES

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ABSTRACT

Assessing the influence of an environmental agent on public health is a difficult multifactorial problem. However, some unifying concepts in research design are now being used to provide a better data base for emission control strategies. The Exposure/Response Matrix is essentially a three-dimensional approach to determining the relationship between environmental stress or insult, and the resulting health effect. One dimension represents pollutant concentration gradient, the second is range of susceptibility within a population and the third is the spectrum of response within population subsets of different susceptibility. This method of approaching study design and interpreted results is applicable to classic toxicology, epidemiology and clinical research.

The pollutant concentration gradient, ranging from background through levels actually occurring in varying geographic areas to those levels recognized as producing overt toxicity must be measured unambiguously and accurately for population studies and reproduced in controlled environmental laboratories for toxicologic and clinical studies. The pollutant gradient or a body pollutant burden is usually treated as the independent variable.

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Humans are not uniformly susceptible to various environmental influences on their health. This normal range of susceptibility must be recognized when characterizing the population in an epidemiologic study, when establishing criteria for subject selection in a clinical study, or when preparing animal models of human disease.

Just as there is a range of susceptibility within the population, there is a spectrum of response within each more or less susceptible subset of the population. The range of response is usually a function of pollutant concentration, duration of exposure, and the presence of co-stressors such as exercise, thermal stress, or other co-existing pollutants.

The final goal of environmental health effects research is the construction of this three-dimensional dose-response relationship to calculate risk factors which reflect the degree of hazard, as well as the size of the population at risk for any set of environmental circumstances.

INTRODUCTION

Modern man is well aware of many stresses and health hazards associated with his rapidly evolving industrial society. These concerns have been expressed in a variety of laws and regulations designed to assure occupational safety and consumer protection over the past several decades. Only relatively recently, however, has a serious attempt been made to protect the general population from harmful effects of existing and emerging industrial and technologic processes.

Complex interactions of environmental factors have focused attention on the necessity for a systematic approach to the evaluation of environmental health hazards. Association of changes in health status with changes in environmental factors is made even more difficult by the complexity of environmental stress in general. It is clear some simplifying concepts must be used to organize and interpret environmental health effects data. These simplifying concepts are also useful in establishing a systematic approach to acquisition of new health effects data.

RANGE OF SUSCEPTIBILITY

Humans are not uniformly susceptible to environmental stress. In epidemiologic studies, greater correlation between pollutant gradient and health effects has been seen in the incidence of respiratory infection in children, in the excess number of asthma attacks, and in excess symptoms in people with cardiopulmonary disease. In clinical research it is evident that persons with arteriosclerotic heart disease are much more susceptible to effects of carbon monoxide than are normal subjects.

In order to make meaningful statements concerning Range of Susceptibility, we must know (1) the nature of the health effect in more or less susceptible individuals, (2) the size of susceptible populations, and (3) their geographic distribution with respect to concentration of pollutants in the environment. Even when health effects for susceptible segments of the population have been determined,

the size and distribution of that segment is usually inadequately known. Not only improved health effects research, but improved national health survey statistics are required to better estimate the influence of environmental factors on public health.

SPECTRUM OF RESPONSE

Whereas there is a range of susceptibility within a population, "spectrum of response" refers to the various ways an individual can manifest the effects of environmental stress. The spectrum of response is usually a function of pollutant concentration, duration and exposure, and the presence of co-stressors such as exercise, thermal stress, or other pollutants. The spectrum has been classified into categories ranging from the mildest to the most severe. They are: (1) pollutant body burden, (2) changes of uncertain significance, (3) pathological changes, (4) morbidity, and (5) mortality. Because the proportion of any population falling into any category is greatest with (1) and the least with (5), it is evident that the concept of "range of susceptibility" is closely related to that of response spectrum. Consideration of the two concepts allows the construction of a three-dimensional dose-response relationship which can be used to calculate risk factors that reflect the degree of hazard as well as size of the population at risk. This kind of prediction is the final goal of environmental health effects research. We are trying to answer the question, "How many individuals in each category of our population are subjected to what levels of risk for a given range of pollutant concentration?"

THE EXPOSURE-RESPONSE MATRIX

The exposure-response matrix uses dose, established by environmental monitoring and modeling or by pollutant burden analysis, as the independent covariate. The two inter-related dependent covariates, as described, are Spectrum of Response and Range of Susceptibility. Without the third covariate, such a plot is simply the classic Dose/Response relationship. With the "z" axis representing the Range of Susceptibility there is additional

information concerning total assessment of risk relating the degree of response at a particular dose to specifically susceptible population subsets.

An example of the Exposure-Response matrix is presented in Table I. Here data concerning the effects of acute carbon monoxide exposure on cardiac function have been used. Range of Susceptibility has been divided into four categories: (A) young normal men, (B) middle-aged normal men, (C) men with pre-clinical or asymptomatic arteriosclerotic heart disease, and (D) men with overt arteriosclerotic heart disease. Spectrum of Response is presented according to the described classification scheme:

- (1) Pollutant burden - carboxyhemoglobin levels above background
- (2) Physiologic changes of uncertain significance - decreased exercise tolerance in young normals, changes in systolic time intervals in middle-aged normals
- (3) Pathologic changes - increased electrocardiographic abnormalities in middle-aged normals and those with pre-clinical as well as overt arteriosclerotic heart disease
- (4) Morbidity - restriction of activity in patients with angina pectoris
- (5) Mortality

Reasonable estimates for the size of the population at risk can be made for each of the five categories:

- (1) Pollutant burden - A recent survey in the United States has indicated that 45% of the non-smoking population had carboxy-hemoglobin concentrations greater than 1.5%
- (2) Physiologic changes of uncertain significance - those changes seen in young normals apply to the entire population. Those seen in middle-aged normals apply to that fraction 40 years old or greater (35% of the US population)
- (3) Pathologic changes - those seen in middle aged normals includes that part of the population with either pre-clinical or overt arteriosclerotic heart disease

TABLE I

Range of Susceptibility	Spectrum of Response	COHb%			
		0-5	5-10	10-15	15-20
A	1	+	+	+	+
	2	+	+	+	+
	3	-	-	0	0
	4	-	-	0	0
	5	-	-	-	-
B	1	+	+	+	+
	2	+	+	+	+
	3	-	-	0	0
	4	-	-	0	0
	5	-	-	0	0
C	1	+	+	+	+
	2	+	+	+	+
	3	+	+	0	0
	4	-	-	0	0
	5	-	-	0	0
D	1	+	+	+	+
	2	+	0	0	0
	3	+	0	0	0
	4	+	0	0	0
	5	-	0	0	0

+ = effect seen
 - = no effect
 0 = inadequate data

- (4) Morbidity - Patients with angina pectoris comprise about 2.1% of the US population. About 5% have definite or suspect coronary artery disease.
- (5) Mortality - Although some studies show a relationship between ambient carbon monoxide levels and excess mortality in hospitalized patients, other studies have not shown such a relationship. Relationships expressed in Table I are appropriate only for acute exposures and do not consider the problem of chronic carbon monoxide intoxication.

No systematic scheme to derive a numerical score for a matrix such as that presented in Table I has yet been developed. Such a scheme would be very useful in assessing the adequacy of the data base for any environmental standard. A more sophisticated and powerful approach is the use of these data to calculate a damage function. Such a function will be most useful in performing Cost/Benefit analysis to optimize environmental control. This function could take the following form:

$$(1) D = f(X_1, X_2, \dots, X_i, \dots, X_k)$$

$$(2) X = g(S, R, \xi)$$

$$(3) R = h(r_1, r_2, r_3, r_4, r_5)$$

$$(4) \xi = j(E_1, E_2, \dots, E_i, \dots, E_j)$$

$$(5) E = q(e, p)$$

$$(6) e = m \int_0^{\cdot} de'/dt$$

$$(7) p = n(r_1, r_2, r_3, r_4, r_5)$$

Where:

D = Overall population damage function

X = Population subset damage function

S = Categories of susceptibility

- R = Response spectrum for each S_i
- ξ = Exposure density function for each population subset $S_{ij}R_{ij}$
- E = Dose frequency distribution for each geographic area under consideration
- e = Exposure integral (dose) for each population risk subgroup, p_i
- e' = Air quality data bits
- p = Population risk subgroup function based on size of population in each response spectrum category with a weighting factor for degree of injury in each category

The elements of these equations identify many components of a useful analysis. Currently available environmental monitoring data as well as health effects data are still inadequate for such a multivariate analysis to be meaningful. Derivation of such an equation is not an empty academic task, however, if it serves to focus attention on the problems of comprehensive environmental analysis.

CONCLUSIONS

Evaluation of various environmental control strategies ideally incorporates an analysis of costs of control compared to health benefits of improved environmental quality. Cost estimates, especially when projected over a ten or twenty year period, may suffer from inadequate technical information. Estimation of health benefits, however, suffers from conceptual as well as technical inadequacies. A three-dimensional Exposure-Response Matrix is presented as a basis for improving synthesis of a human health damage function as well as providing a better framework for controlled environmental laboratory studies.

DISCUSSION

GOLDSMITH (U.S.A.)

In the presentation of the model is it not too elaborate to assume that for each population subset there are a large number of response variables (r_n) when in most population subsets only one or rarely two are likely to be observed.

Our colleagues, especially those in Sweden, have demonstrated that annoyance reactions are common, readily measured, and in our experience a very common health complaint. I include eye irritation, respiratory irritation, sense of difficulty in breathing, and possibly tangentially, noise annoyance. I believe that these effects are considered by the public to be health effects; why do you and Drs. Jackson and Newill exclude annoyance reactions from population health responses? In doing so, do you not imply that these reactions have no long-term disease or disability implications? On what basis can we assume that these annoyance reactions are not associated significantly with risk of increased body burden, physiological impairment, or pathological changes?

The assumption that costs of medically measurable effects are more readily measured than annoyance reactions is very shaky. Costs of change of residence, loss of property value, and demands for relief and abatement are readily measured costs, compared to these, costs of increased body burden, abnormality of ECG, or even impairment of exercise capacity in angina patients, are difficult to assign a dollar value to.

KNELSON (U.S.A.)

I share Dr. Goldsmith's concern with the complexity of the general damage function presented. However, it is the advantage of using symbolic notation, that one can render very complex relationships relatively comprehensible. Compared to the real world, the list of formulae I have proposed are simplistic. Including dose response variables for population subsets with respect to range of susceptibility as well as spectrum of response is necessary to show the interaction between these two interdependent vectors in defining the size and nature of the population at risk.

With respect to Dr. Goldsmith's second statement, I do not assume that medical effects are more easily measurable than nuisances. I simply have no experience with the latter problem and am therefore not competent to discuss it. I am sure, however, that others could provide the necessary data for inclusion in a more general statement of damage.

DEAN (Ireland)

We are taking part in a week's symposium on the Health Effects of Environmental Pollution involving over 200 papers. No paper considers the greatest threat of environmental pollution which is radiation, perhaps from a limited nuclear war.

Should we not include in our discussions how the human race can survive the environmental pollution which may result from a sudden increase in radiation, - and as a corollary express our concern at the failure to restrict preparations for a nuclear missile war or the inadvertant release of a massive amount of radiation?

KNELSON (U.S.A.)

I am sure we all share your concern. However, in the context of this symposium it seems to me impossible to even begin to deal with the important issue you have raised.

(EDITORIAL NOTE: It was a decision of the Organizing Committee not to include the topic of risks due to ionizing radiation in this Symposium in view of the many meetings devoted to this subject. Furthermore, several specialized international organizations are now reviewing these risks.)

SCHLIPKÖTER (Federal Republic of Germany)

When setting threshold values two points are difficult to judge:

1. What importance must be attached to odour annoyance and irritation effects? Irritation effects should be regarded as having negative effects on health. Do you agree with this standpoint?
2. How should subjects with previous damage (illnesses) be considered? Which illnesses and degree of illness should still be taken into consideration? If persons with severe emphysema or bronchitis were included the threshold values would have to be very low.

KNELSON (U.S.A.)

1. Dr. Schlipköter has raised the question of quantitating the nuisance aspects of environmental stress. This problem has been approached by several groups of investigators, usually employing a subjective ranking score. I agree with the importance both you and Dr. Goldsmith attach to annoyances, irritation syndromes and what might be referred to as interference with quality of life in general. I

believe these aspects of environmental stress can be included in the overall damage function I have defined.

2. I agree also with Dr. Schlipkötter's concern with exacerbation of chronic illness related to environmental factors. It is precisely interactions of this sort that should be recognized in the overall assessment of a general damage function. As you know, in the United States we do recognize the need to protect particularly susceptible segments of the population. This principle is most evident with respect to CO and coronary artery disease. We have described the exacerbating effect of respirable sulfates on asthmatics and have work in progress concerning the effects of nitrogen dioxide and ozone on persons with chronic lung disease.

DOSE-RESPONSE RELATIONSHIPS LINKING SHORT-TERM
AIR POLLUTION EXPOSURES TO AGGRAVATION
OF CARDIO-RESPIRATORY ILLNESS

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ABSTRACT

In 1970 and 1971, the US Environmental Protection Agency conducted several epidemiologic studies which assessed the effects on human health of day-to-day fluctuations in air pollution levels. Three of these studies are summarized in this report. Two studies, one in the New York City metropolitan area and one in Utah's Salt Lake Basin, investigated pollution effects in groups of asthmatic children and adults. The third, in the New York area, investigated pollution effects in groups of elderly patients with combined cardio-pulmonary disease. In all studies, subjects maintained symptom diaries for about eight months. A total of 359 asthmatics and about 200 elderly patients participated.

In Utah, outdoor temperature showed a strong negative correlation with asthma attack rates. On subfreezing days, the temperature effect was strong enough to obscure any pollutant effects that may have been present. On days of minimum temperature between 30° and 50° Fahrenheit, attack rates increased consistently as total suspended particulate (TSP) levels increased. On days of minimum temperature above 50°, attack rates increased consistently as both TSP and suspended sulfate (SS) levels increased. Levels of SS, above which excess attacks could be

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expected, were estimated at $17.4 \mu\text{g}/\text{m}^3$ for days of minimum temperature between 30° and 50° , and at $1.4 \mu\text{g}/\text{m}^3$ for warmer days.

In New York, as in Utah, the estimated SS threshold for excess asthma attacks was lower on days of minimum temperature above 50° than on cooler days ($7.3 \mu\text{g}/\text{m}^3$ and $12 \mu\text{g}/\text{m}^3$ respectively). Effects of temperature and pollution on asthma attack rates were generally not as strong in New York as in Utah.

In cardio-pulmonary patients, decreasing temperatures promoted increased rates of aggravation of symptoms. The effects of pollution on cardio-pulmonary symptoms were slightly stronger on cold days than on warmer days. The level of SS above which excess symptom rates could be expected was estimated at $9.2 \mu\text{g}/\text{m}^3$ for days of minimum temperature between 20° and 40° . For warmer days, a reliable point estimate of the SS threshold could not be made.

1. Introduction

This report will summarize the results of three epidemiologic studies,^{1,2,3} conducted by the U.S. Environmental Protection Agency (EPA). Two studies tested the hypothesis that daily changes in ambient air pollution directly affect the frequency of asthma attacks. The third study tested the hypothesis that daily changes in ambient air pollution directly affect the severity of symptoms of chronic cardio-pulmonary disease. Each of the three studies was the first of a series in its area. One study of asthma was performed in the Salt Lake Basin in Utah, in the Western United States, where the major pollution source is a large copper smelter. The major pollutants in this area are oxides of sulfur, specifically suspended sulfates and sulfur dioxide. Two studies, one of asthma and one of chronic cardio-pulmonary disease, were performed in the New York City Metropolitan Area, where the major pollutants are oxides of sulfur and suspended particulate matter.

2. Methods

In New York and Utah, asthmatics and cardio-pulmonary patients were identified and enrolled through clinical records, health questionnaire information, and house-to-house interviews. Asthmatics were eligible for study if they had had at least one asthmatic attack in the past year, and if their attacks involved, at a minimum, wheezing and shortness of breath. Both children and adults were enrolled in the asthma studies. Patients with chronic cardio-pulmonary disease were all at least 60 years old, and had had their illness diagnosed by a doctor.

The Utah asthma study was conducted in four communities of different sulfur oxide exposures. The New York asthma and cardio-

pulmonary studies were each conducted in three communities of different sulfur oxide and particulate exposures. Two communities were within the New York City limits; the third was on suburban Long Island. Air monitoring stations were installed in residential areas in each community. Daily measurements of sulfur dioxide, suspended sulfates, and total suspended particulates were obtained from each station. Each study participant lived within two miles of his community's air monitoring station. In all three studies, study participants used self-administered symptom diaries to report asthma attack frequency or cardio-pulmonary symptom severity. In Utah, data were collected during the 26-week period from March 7, 1971 through September 4, 1971. In New York, data were collected during the 32-week period from October 3, 1970 through May 23, 1971. In each community in Utah and New York, about 50 asthmatics were enrolled. In the New York cardio-pulmonary study, a total of about 200 participants were enrolled.

3. Results

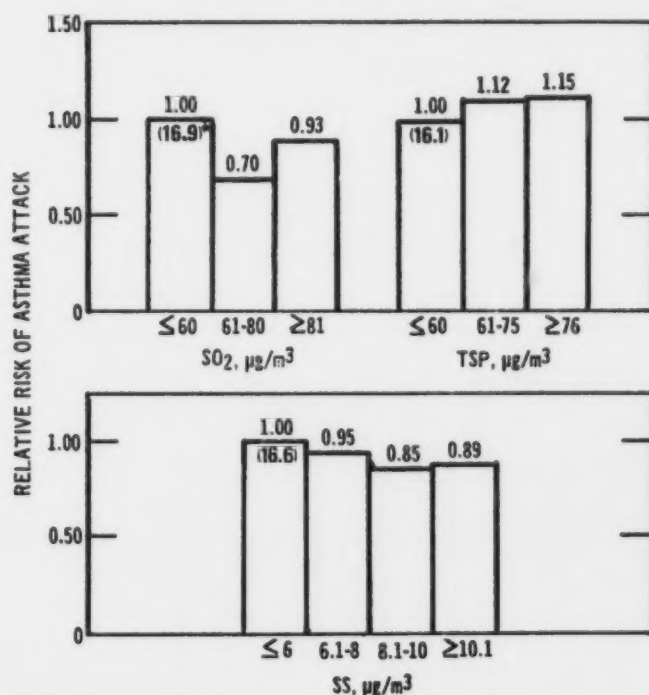
3.1 Utah Asthma Study

In the Utah asthma study, the frequency of attack rates was more strongly and consistently correlated to minimum daily temperature than to any other environmental variable. As temperature decreased, attack frequency increased. Indeed, on subfreezing days (minimum temperature below 30°F), no effect of air pollution on attack rates could be detected.

On days of minimum temperature between 30 and 50°F, increases in asthma attack rates were associated consistently with increases in total suspended particulates (TSP). For all days in this temperature range on which the daily average TSP level was at or

below $60 \mu\text{g}/\text{m}^3$, the asthma attack rate was 16.1 attacks per hundred person-days of diary coverage. (In other words, for each 100 diaries from days having these temperature and pollution conditions, 16.1 diaries would report one or more asthma attacks.) When TSP levels rose to $61-75 \mu\text{g}/\text{m}^3$, the attack rate rose by 12%, to 18.0. On days having TSP levels of at least $76 \mu\text{g}/\text{m}^3$, the attack rate rose by an additional 3%, to 18.5 (Figure 1). On days of minimum temperature between 30 and 50°F , increases in sulfur dioxide (SO_2) and suspended sulfates (SS) were not consistently associated with increased attack rates.

UTAH, 1971: RELATIVE RISK OF ASTHMA ATTACK ON DAYS OF LOW AND HIGH EXPOSURES TO SO_2 , TSP, AND SUSPENDED SULFATES, (MINIMUM TEMPERATURE 30 TO 50°F)



* Baseline attack rates in parentheses

FIGURE 1

On warmer days, of minimum temperature above 50°F, increases in both TSP and SS were consistently associated with increased attack rates (Figure 2). When TSP levels were below 60 $\mu\text{g}/\text{m}^3$ on such days, the attack rate was 12.1 attacks per 100 person-days. When TSP increased to 61-75 $\mu\text{g}/\text{m}^3$, the attack rate rose by 8%, to 13.1. When TSP levels were above 75 $\mu\text{g}/\text{m}^3$, the attack rate rose by 17% above the baseline level, to 14.2. On warmer days, only

UTAH, 1971: RELATIVE RISK OF ASTHMA ATTACK ON DAYS OF LOW AND HIGH EXPOSURES TO SO_2 , TSP, AND SUSPENDED SULFATES (MINIMUM TEMPERATURE $\geq 51^\circ\text{F}$)

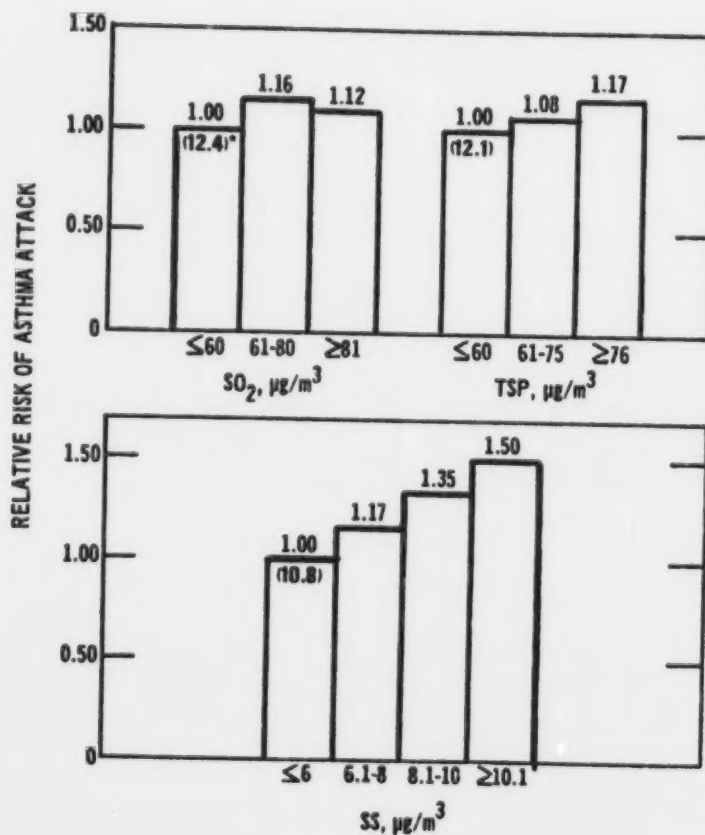


FIGURE 2

* Baseline attack rates in parentheses

small increases in attack rates were observed with increasing SO_2 levels.

Attack rates rose most sharply and consistently with increasing SS levels on warm days. When SS were below $6 \mu\text{g}/\text{m}^3$ on such days, the attack rate was 10.8 attacks per 100 person-days. When SS increased to $6-8 \mu\text{g}/\text{m}^3$, the attack rate rose by 17% to 12.6. When SS increased to $8-10 \mu\text{g}/\text{m}^3$, the attack rate increased by an additional 18%, to 14.6. Finally, on warmer days when SS levels exceeded $10 \mu\text{g}/\text{m}^3$, the attack rate was 16.2. This figure represents an increase in attack rate of 50% above days when sulfate levels were below $6 \mu\text{g}/\text{m}^3$.

Least squares estimation techniques were applied to the Utah data to determine threshold levels of SS above which excess asthma attacks could be expected (Figure 3). Estimates indicated that on days of minimum temperature between 30 and 50°F , excess attacks might not be expected until SS levels reached $17.4 \mu\text{g}/\text{m}^3$. On warmer days, excess attacks might be expected when SS exceeded the very low level of $1.4 \mu\text{g}/\text{m}^3$.

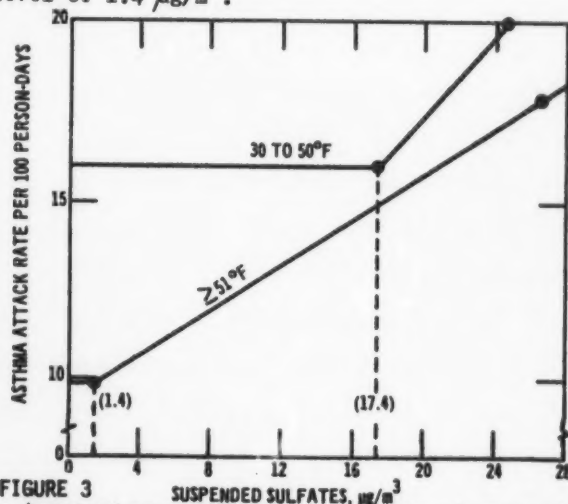


FIGURE 3
Utah, 1971: temperature - specific estimates of suspended sulfate levels above which excess asthma attacks occur.

4. Discussion

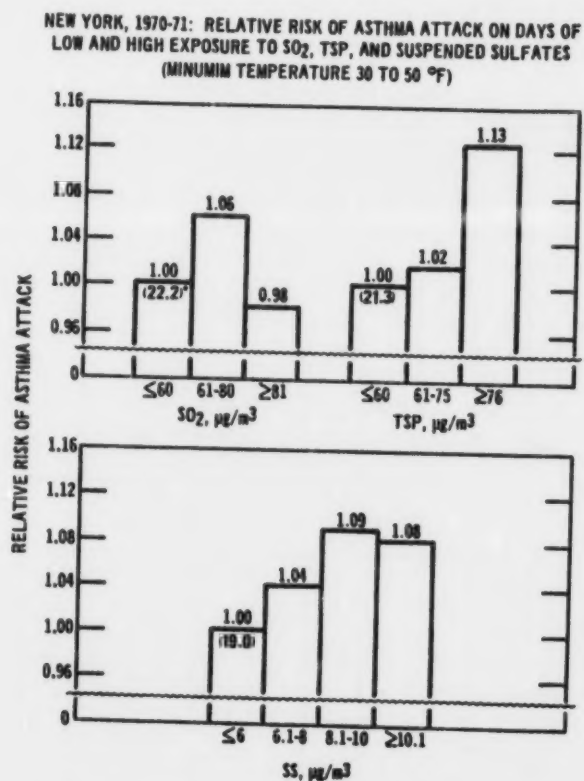
Each of the three studies described in this report was the first of a series. Clearly, the findings of each study require verification by the subsequent studies in its series. However, the studies described here stand alone in identifying SS as a pollutant of major concern. On the basis of the findings described, the investigators felt that adverse effects on both asthma and combined cardio-pulmonary disease might be expected when daily average SS levels reach $8-10 \mu\text{g}/\text{m}^3$ or above. In American cities, daily SS levels exceed $8-10 \mu\text{g}/\text{m}^3$ a substantial proportion of the time. Indeed, during the fall and winter of 1971, SS levels exceeded $8-10 \mu\text{g}/\text{m}^3$ over 50% of the time in one of Utah's study communities. During the period of study in New York City, daily SS levels exceeded $8-10 \mu\text{g}/\text{m}^3$ 70% of the time.

The threshold SS estimate of $8-10 \mu\text{g}/\text{m}^3$ may in fact be higher than the true threshold in some geographic areas. Theoretical and empirical considerations support this point. Theoretically, it is thoroughly conceivable that, with increased knowledge and investigative skill, scientists will detect adverse health effects in the future at near-zero concentrations of SS and other pollutants. Empirically, the low threshold SS level of $1.4 \mu\text{g}/\text{m}^3$ was estimated from the data collected from Utah asthmatics on warm days.

There are at least three possible explanations for the observed discrepancy between the New York and Utah threshold estimates. First, the reporting habits of asthmatics may have been different in the two areas. Second, the least squares estimation techniques yielded broad confidence limits around the point estimates of thresholds. We cannot state unequivocally

3.2 New York Asthma Study

In New York, asthma attack rates were generally higher than in Utah. This difference probably reflects differences in the original composition of study samples rather than more severe pollutant effects in New York than in Utah. In fact, neither temperature nor pollution exerted effects on attack rates in New York as strongly or consistently as they did in Utah. In New York, on days of minimum temperature between 30 and 50°F, attack rates generally increased with increasing TSP and SS levels (Figure 4).



*Base attack rates in parentheses

Figure 4.

On such days, the attack rate rose from 21.3 attacks per 100 person-days when TSP levels were below $61 \mu\text{g}/\text{m}^3$, to 24.1, an increase of 13%, when TSP levels exceeded $76 \mu\text{g}/\text{m}^3$. On days in the same temperature range, the attack rate rose from 19.0 when SS levels were below $6.1 \mu\text{g}/\text{m}^3$, to 20.7, an increase of 9%, when SS levels were between 8 and $10 \mu\text{g}/\text{m}^3$. When SS levels exceeded $10 \mu\text{g}/\text{m}^3$, a very slight fall in the attack rate (1%) was observed.

On warmer days in New York, when the minimum temperature exceeded 50°F , the attack rate continued to increase with increasing SS levels (Figure 5). On such days the attack rate rose by 10%, from 22.1 attacks per 100 person-days when SS levels were below $8 \mu\text{g}/\text{m}^3$, to 24.3 when SS levels exceeded $10 \mu\text{g}/\text{m}^3$. On these

NEW YORK, 1970-71: RELATIVE RISK OF ASTHMA ATTACK ON DAYS OF LOW AND HIGH EXPOSURE TO SO_2 , TSP, AND SUSPENDED SULFATES (MINIMUM TEMPERATURE $\geq 51^\circ\text{F}$)

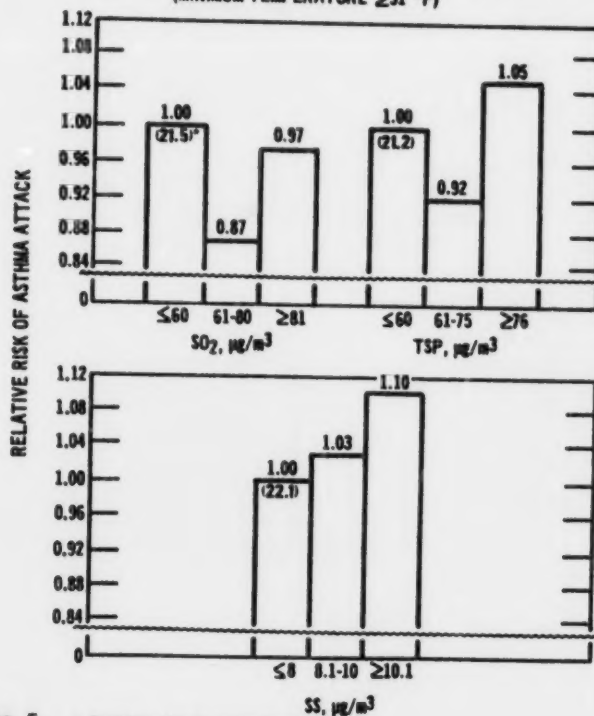


Figure 5. * Baseline attack rates in parentheses

warmer days, the attack rate did not increase consistently with TSP levels.

No consistent effect of SO_2 on attack rates was observed in New York in either temperature range.

Estimates of threshold SS effects on attack rates were developed from the New York data (Figure 6). As in Utah, the SS threshold was higher in New York on warm days than cooler ones ($11.9 \mu\text{g}/\text{m}^3$ and $7.3 \mu\text{g}/\text{m}^3$, respectively). The difference in temperature-specific threshold estimates was not as great, nor was the warm-temperature threshold estimate as low, in New York as in Utah.

NEW YORK, 1970-71: TEMPERATURE-SPECIFIC ESTIMATES OF
SUSPENDED SULFATE LEVELS ABOVE WHICH EXCESS ASTHMA
ATTACKS OCCUR

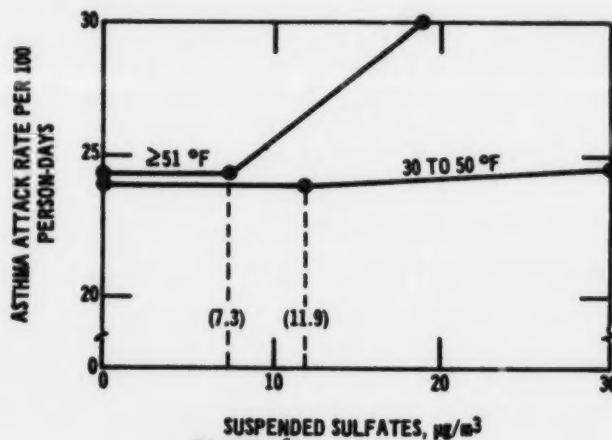
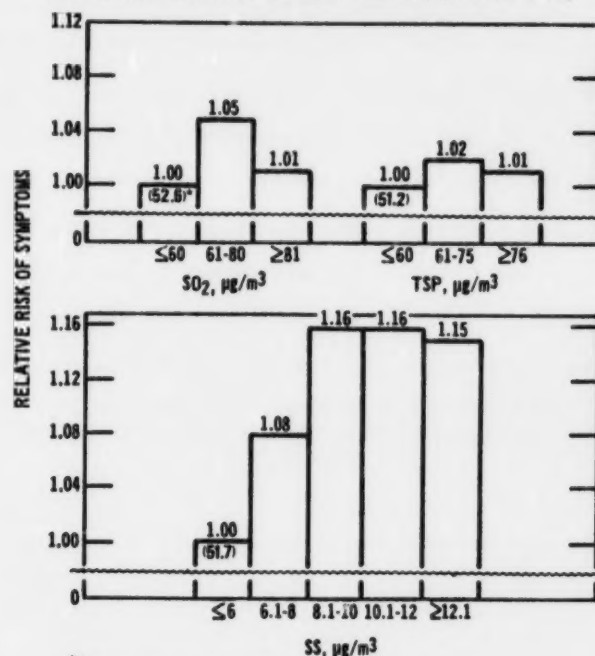


Figure 6.

3.3 New York Study of Cardio-Pulmonary Disease

For cardio-pulmonary patients in New York, decreasing temperatures were strongly associated with increased frequency of aggravation of symptoms. On days of minimum temperature between 20° and 40°F , the frequency of aggravation rose quite steadily as SS levels increased (Figure 7). On such days, the rate of symptom

NEW YORK, 1970-71: RELATIVE RISK OF CARDIO-PULMONARY SYMPTOM AGGRAVATION ON DAYS OF LOW AND HIGH EXPOSURES TO SO_2 , TSP, AND SUSPENDED SULFATES (MINIMUM TEMPERATURE 20 TO 40 °F)



*Base attack rates in parentheses
Figure 7.

aggravation was 51.7% when SS levels were $6 \mu\text{g}/\text{m}^3$ or below. When SS levels were between 8 and $12 \mu\text{g}/\text{m}^3$, the aggravation rate increased by 16% to 59.5%. When SS levels were above $12 \mu\text{g}/\text{m}^3$, the aggravation rate declined very slightly (1%) to 59.0%. On these cooler days, elevations in symptom severity associated with rising TSP and SO_2 were small, 5% at most, and not very consistent.

On warmer days, of minimum temperature above 40°F, there was also a distinct tendency toward increased frequency of symptom aggravation as SS levels increased (Figure 8). The aggravation rate was 46.8% when SS levels were $6.0 \mu\text{g}/\text{m}^3$ or less. When SS levels rose to $10-12 \mu\text{g}/\text{m}^3$, the aggravation rate increased 17%, to 54.8%.

NEW YORK, 1970-71: RELATIVE RISK OF CARDIO-PULMONARY SYMPTOM AGGRAVATION ON DAYS OF LOW AND HIGH EXPOSURES TO SO_2 , TSP, AND SUSPENDED SULFATES (MINIMUM TEMPERATURE $\geq 41^\circ\text{F}$)

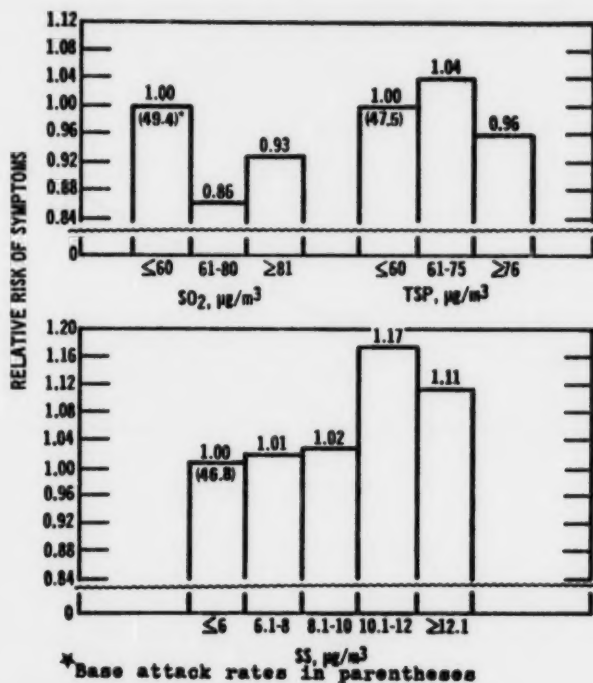


Figure 8.

When SS levels were above $12 \mu\text{g}/\text{m}^3$, there was a slight (6%) decline in the aggravation rate. On warmer days, there were no consistent elevations in symptom severity associated with increasing TSP and SO_2 levels.

The ambient level of SS at which elevated rates of symptom aggravation could be expected were estimated by least squares estimation techniques. For cardio-pulmonary patients on days of minimum temperature between 20 and 40°F , this estimated SS level was $9.2 \mu\text{g}/\text{m}^3$. For warmer days, a reliable point estimate of a threshold could not be made.

NEW YORK, 1970-71: ESTIMATE OF SUSPENDED SULFATE LEVEL
ABOVE WHICH CARDIO-PULMONARY SYMPTOM AGGRAVATION OCCURS

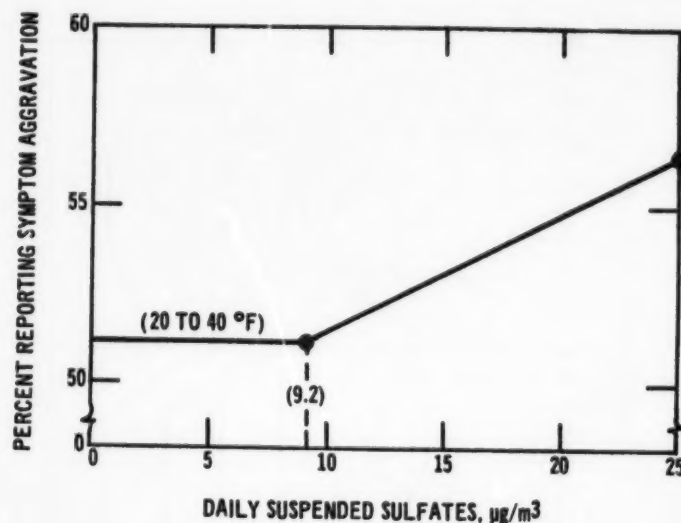


Figure 9.

that the thresholds estimated for Utah and New York were significantly different from each other. Third, the lower threshold in Utah may indicate that the physical and chemical composition of SS in Utah's atmosphere was different from that in New York's. These possibilities are currently being tested.

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DISCUSSION

MAGE (Denmark)

Is it not correct that daily suspended sulphates at 0 mg/m^3 must give zero excess attacks? If as you state that the "noise" in the data prevent you from discerning the lower portion of the curve, what justification is there for drawing the curve as horizontal? Why did not the study filter this "noise" out from the data? You define excess asthma attacks in a nonspecific manner, since your basis is not defined for what constitutes zero excess attacks.

CHAPMAN (U.S.A.)

The hockey stick function is an expression of simple attack rates, not "excess attack" rates. The zero line for "excess attacks" would be the same line as the horizontal portion of the hockey stick function. In that sense, the hockey stick function does indeed intersect "excess attacks" at zero.

Clearly, in any population of active asthmatics, there will be attacks even in the complete absence of sulfates. This is unavoidable. Thus, the hockey stick function does not, indeed cannot, intersect the zero line for simple attack rate.

HINE (U.S.A.)

1. Is the concept of the continuum of effects rather than the use of the classic dose-response curve on a political, sociological or biological basis?
2. Were the differences shown statistically significant for increased responses by the asthmatics in Salt Lake and New York?
3. Is there a plateau effect with increased levels of pollutant as regards responses of the selected population?
4. Is there a lower arm to your sigmoid curve?

CHAPMAN (U.S.A.)

1. We have certainly not ruled out the possibility that classic dose-response curves exist for many pollutants. It does seem reasonable, though, on a biologic basis, that as health indicators become more and more sensitive, effects will be observed at lower and lower pollution levels.
2. In addition to the temperature-specific relative risk models presented, simple correlation and stepwise multiple regression analyses of these data were performed. Correlation and regression coefficients were generally not statistically significant for SO_2 and TSP, but were quite consistently significant for sulfates.
3. The plots of relative risk for the New York asthma and cardio-pulmonary studies (Figures 4, 7 and 8) suggest that there may be a "plateau effect" for sulfates. This finding definitely requires verification in replicate studies.
4. To date, we have not made detailed analyses of the lower end of the exposure spectrum. However, the presence of a horizontal portion at the lower end of most of our threshold estimation functions to date suggests that, for the parameters studied, there may be a lower horizontal portion in the dose-response curves.

PHAM (France)

1. Your paper raises the problem of the use of health indicators. You used the number of attacks registered by the subjects as an indicator. What effect would the treatment that these subjects could receive have on subsequent attacks?
2. If you use a bronchial susceptibility test (for example, measurement of change in air way resistance) would it not lower the observed thresholds?

CHAPMAN (U.S.A.)

1. You are raising a problem that is most pertinent, and most difficult to control for. I believe that, in most cases, the attack rate in a treated asthmatic would be lower than the rate in the same patient if he were untreated. Many of the asthmatics in our studies routinely take some sort of preventive medication, so that the attack rates that we publish might best be considered minimum attack rates.

It seems unlikely to me that medication taken to relieve an attack in progress would have much effect on the incidence of future attacks, since the duration of activity of routine asthma medication is usually quite short. However, I also believe one

could argue that present medication might affect future attack rates positively or negatively. To my knowledge, few data are available on this point.

In our studies of asthma, we ask all patients daily whether they have taken medication for asthma, and whether they have taken more or less medication than usual. In general, the proportion of patients taking medication differs little from community to community. Whatever effect medication might have on attack rates probably is distributed evenly in all communities. Thus, though our published attack rates may be low, our conclusions about attack rates in one community relative to another are probably valid.

2. It is very difficult to say whether pulmonary tests would have been more sensitive indicators than number of attacks, since few data are as yet available on this point. In the next year, EPA will be testing the sensitivity of just such indicators as you have suggested.

BULCRAIG (U.K.)

As a chemist I feel it is essential to distinguish between neutral sulphates and acid sulphates in studies of the relationship of diseases to SO_2 and suspended sulphates. It is well known that SO_2 is oxidised to sulphate in perhaps 2 or 3 days but there are ample data in the United Kingdom to show that the endproduct is mainly ammonium sulphate or sodium sulphate. Sulphuric acid has been found in foggy conditions, and the Threshold Limit Values recommended by the U.S.A. Association of Industrial Hygienists and the UK Department of Health show that SO_3 or sulphuric acid are rated as 12 times more toxic than SO_2 while neutral sulphates are not even included in the list of substances for which a TLV is recommended. I therefore regard as essential to measure the acidity as well as the total of suspended sulphates. This might explain the significant difference between Utah and New York since Dr. Chapman mentioned the existence of a large smelter in Utah and furnaces often emit a higher proportion of SO_3 to SO_2 whereas in New York the sulphates may be mainly neutral as in most cities in the U.K.

Chemically it would not be difficult to measure both factors and until this is done one cannot be sure of the interpretation of the apparent relationship of the diseases to total suspended sulphates.

CHAPMAN (U.S.A.)

I agree wholeheartedly with your general point, that complete chemical and physical characterization of local sulfates is an extremely important goal. One should bear however, in mind that certain metal sulfates such as zinc ammonium sulfate can cause increased airway resistance in animals. Thus, even metal sulfates may exert toxic effects in human populations.

EFFECTS OF SOME APPROXIMATIONS IN ANALYSES OF RADIOLOGICAL RESPONSE TO COALMINE DUST EXPOSURE

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ABSTRACT

Problems of analysing incomplete epidemiological data to provide guidance on coalmine dust standards are considered. An interim analysis of results from a longitudinal study in British mines had provided estimates of probabilities of developing various degrees of coalworkers' pneumoconiosis following exposure to different concentrations of respirable dust. These dose response relationships were used to guide decisions on dust standards. Data which became available subsequently have permitted quantitative assessments of how certain approximations used for the interim analysis affected results.

Averages of dust concentrations at coalfaces sampled in a colliery during a ten year period proved to be good estimates of average cumulative dust exposures of face workers in the collieries. However, re-grouping data according to men's individual dust exposures showed that attribution of a single (mean) dust-dose to men working in the same colliery introduced a bias into the analysis. Risks associated with high dust concentrations had been overestimated; at lower concentrations they had been underestimated, to a lesser extent. A simplified stochastic model of radiological progression was used in the interim analysis to permit temporal extrapolation of results. This took no formal account of variations in dust exposure prior to the research.

Later calculations give more variable results, but provide no evidence of serious bias arising from the simplifying assumption. An earlier finding concerning higher risks of radiological response to dust among men with pneumoconiosis is confirmed. The practical importance of this observation is discussed.

1. Introduction

Use of epidemiological data as a guide to decisions on permissible levels for pollutants presupposes relevance of study designs to the problem of interest and the use of valid methodology. Even when these conditions are met, difficulties arise if specific action is required before an epidemiological study is complete, and guidance is sought from the incomplete data. The plausibility of assumptions used to interpret the data may rest partly on informed value judgements rather than on the results available; but inherent in this situation is the opportunity to study the effects of approximations as more data become available.

Such was the case in the period leading to the introduction of gravimetric standards for airborne dust in British coalmines in 1970. An interim analysis of results from a longitudinal study in the mines provided estimates of probabilities of developing various degrees of coalworkers' pneumoconiosis following exposure to different concentrations of respirable dust (Jacobsen *et al* [1]). Application of these results to conditions in British coalmines, to assess likely effects of different possible dust standards, required a number of operational assumptions. The data justifying them have been described by Chamberlain *et al* [2]. Consequences of possible deviations from conditions assumed have been discussed quantitatively by Jacobsen [3]. The present paper is concerned with some other approximations which were necessary to derive the probability relationships themselves.

2. Research aims and methods

The Pneumoconiosis Field Research began in 1952 with two main aims: to establish what kinds of dust cause pneumoconiosis and to determine what environmental conditions should be maintained if mineworkers are not to be disabled by the dust they breathe. The research design has been described fully by Fay and Rae [4]. In essence the plan was to take full-size chest X-rays of all working miners in 25 collieries at five-year intervals. About 30 000 men were involved at any one time and the response rate was consistently higher than 90 percent. The collieries were selected from all the British coalfields to provide a representative range of environmental conditions that might prove to be important in the development of pneumoconiosis. Research investigators stationed

permanently at the collieries carried out a statistically designed programme of dust sampling close to the workmen in defined occupational groups. Records were accumulated of the time spent by each man in these groups and occupational histories prior to the research were compiled by interview for all men surveyed. In this way it was hoped to establish a quantitative relationship between radiological appearances and individuals' dust exposures.

3. The interim study

3.1 Objective

The first British coalmine dust standards had been expressed in terms of the number of particles in the size range 1 to 5 μm per cm^3 of sampled air and were measured using the Standard Thermal Precipitator. New dust sampling instruments had been developed by the late 1960s which measured the mass concentration of respirable dust. This was the preferred measure of the medical hazard (Bedford and Warner [5]; Hamilton and Walton [6]) whose use for routine monitoring of dust levels had been postponed only by the earlier non-availability of suitable sampling instruments. The decision by the National Coal Board to introduce gravimetric sampling underground by 1970 determined the objective of the interim study which began in 1967: a relationship between radiological pneumoconiosis and mass concentrations of airborne dust was required urgently to guide the necessary decisions on appropriate new dust standards.

3.2 Data available for first analysis

These are described and discussed in detail by Jacobsen *et al* [7]. The essentials are summarised below.

3.2.1 Radiological

Pairs of X-rays of 4 122 coalface workers employed in 20 of the research collieries were classified for pneumoconiosis by eight doctors experienced in the radiology of pneumoconiosis. Each pair of X-rays represented the start and end of a ten-year period of dust sampling in the collieries concerned. Every doctor examined all pairs. Both films from a pair were classified at the same time using the 12-point scale of abnormality now incorporated in the International Labour Organisation's classification of pneumoconiosis (ILO [8]). The eight classifications of each film were averaged, as described by Jacobsen *et al* [7].

3.2.2 Environmental

The mean dust concentration over all coalface occupational groups sampled over the ten-year period was available for each of the 20 collieries included in the special study. The concentrations were expressed in the units in which they had been measured, that is particles/cm³. These 20 colliery mean concentrations were converted into mass concentration units (mg/m³) using separate factors for each colliery; the factors had been determined experimentally from the results of simultaneous sampling instrument trials in each colliery.

The statistical analyses described by Jacobsen *et al* [7] showed that radiological changes over ten years were correlated with the 20 colliery mean mass concentrations ($r = 0.87$) and the results were used to estimate risks of developing simple pneumoconiosis over periods longer than ten years.

4. Effects of some assumptions

4.1 Use of mean dust concentrations of coalfaces sampled

The mean concentration of all coalfaces sampled in a colliery was taken to be an estimate of the mean exposure for the sample of coalface workers in the colliery. Soon after the original analysis had been reported, calculations of men's individual exposures over the ten years were completed. It transpired that the colliery mean coalface concentrations used in the interim analysis correlated well ($r = 0.94$) with the mean dust exposures of the men studied, although the latter were calculated from detailed records of individual attendance in occupational groups, including some groups away from the coalface. Thus it could be concluded that the positive correlation between radiological results and measures of airborne dust found earlier was not an artefact arising from reliance on results from all coalfaces sampled, as opposed to the individually time-weighted concentrations in groups where the men had been working. Notwithstanding this reassurance, a deviation from linearity in the relationship between the two sets of mean data suggested a possible bias. Fig. 1 shows the relationship between colliery mean results and the mean of concentrations experienced by individuals in those collieries. This figure demonstrates what was not obvious from an earlier analysis by Jacobsen *et al* [7]. A bias in variability about the theoretical straight line which would represent a 1 : 1 relationship

is evident in Fig. 1 at lower as well as at higher concentrations. Thus the data used in the interim analysis appears to have not only underestimated dust levels experienced by individuals at relatively high concentrations but also to have overestimated them at lower concentrations.

Mean Concentrations Experienced
By Individuals (mg/m^3)

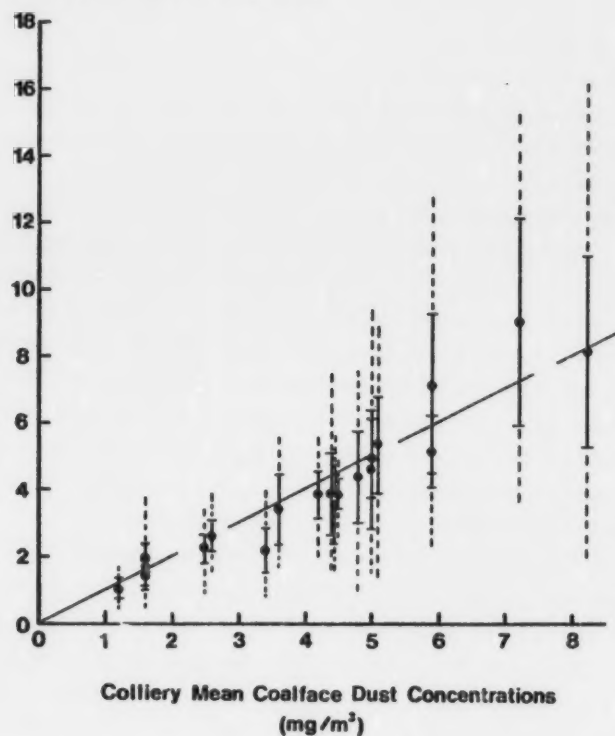


Fig. 1. Variability of mean dust concentrations experienced by individuals in a colliery over ten years in relation to colliery mean coalface dust concentrations.

—SD—●—SD— - - - - -RANGE- - - - -

4.2 Use of colliery mean data instead of individual exposures

The within-colliery variability in Fig. 1 is seen to be an increasing function of the colliery mean concentrations; the highest range of individuals' mean concentrations in one colliery was from 2.1 to 16.1 mg/m^3 . The effect of this variation on the estimated ten-year dose-response relationship has been described by Jacobsen [9]. It is consistent with the bias evident in Fig. 1 but the overestimation of lower concentrations was seen to relate mainly to a minority of the men studied who began the ten-year period with some radiological evidence of pneumoconiosis. Not discussed previously is the question of how the revised ten-year dose-response relationships affect temporal extrapolations of results which were made in the original analysis. Jacobsen *et al.* [8,7] had produced estimates of dose-related risks of developing category 2 or higher simple pneumoconiosis over a 35-year working life at the coalface. These estimates have been used to determine the likely long-term effects of dust standards both in the UK (Jacobsen [3]) and in the USA (Doyle [10]). Table I compares estimates of risks over 35 years. Those relating to concentrations experienced by individuals have been calculated in the same way as that used in the earlier analysis of colliery mean coalface concentrations, but results from the same 4 122 men concerned have been re-grouped according to convenient ranges of individually experienced mean concentrations. In the middle region of the concentrations experienced the estimates are similar. The bias arising from calculations based on colliery mean dust concentrations affects mainly the estimated risks at higher concentrations. This is seen more clearly from Fig. 2 where smooth curves have been fitted to the results (using the angular transformation of estimated probabilities). At 4 mg/m^3 the two curves give the same probability estimates. At 8 mg/m^3 the difference amounts to 0.08 probability units.

4.3 Assumption of a Markov model for temporal extrapolation of radiological results

4.3.1 The model

A third possible source of bias in the previously published results arises from some assumptions used to produce the 35-year-risk predictions from data relevant to 10-year periods. The model depicts changes in the

Table I. Estimates of probabilities of developing category 2 or higher simple pneumoconiosis during a 35-year working life under various dust conditions

- a. using colliery mean dust concentrations
 b. using mean concentrations experienced by individual men in the collieries.

a. Men grouped according to collieries			b. Men grouped according to individual exposures				
Colliery	Number of men	Mean dust conc. (mg/m ³)	Probability estimates		Dust concentration (mg/m ³)		Number of men
			a.	b.	Mean	Range	
S	129	1.2	0	0	1.10	0.5-1.5	348
D	113	1.6	0	0	1.72	-2.0	427
O	319	1.6	0	0.0080	2.21	-2.5	510
P	234	1.6	0				
C	215	2.5	0.0036	0.0140	2.68	-3.0	430
G	268	2.6	0.0069	0.0270	3.20	-3.5	301
J	254	3.4	0.0074	0.0354	3.70	-4.0	350
I	161	3.6	0.0077				
B	211	4.2	0.0212				
M	261	4.4	0.0420	0.0744	4.18	-4.5	355
E	76	4.4	0.0185	0.0486	4.71	-5.0	291
X	160	4.5	0.0484				
T	281	4.8	0.0509				
W	99	5.0	0.0448	0.0387	5.19	-5.5	243
Y	293	5.0	0.0454				
V	335	5.1	0.0456				
L	196	5.9	0.1107	0.0373	5.91	-6.5	335
Q	291	5.9	0.1000				
A	80	7.2	0.1428	0.0394	6.95	-7.5	227
F	146	8.2	0.2095	0.1608	9.47	>7.5	305
Total	4122						4122

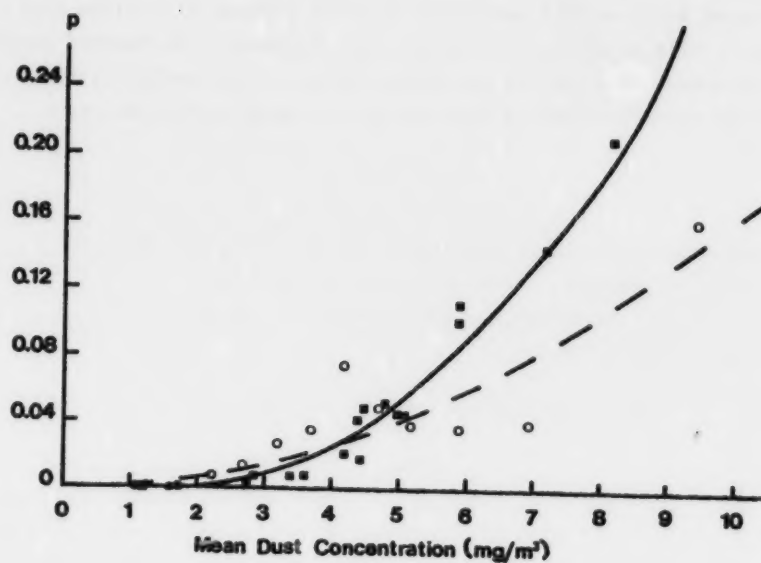


Fig. 2. Bias arising from use of colliery mean data as estimates of individual exposures. Fitted curves to estimates of probabilities of developing category 2 or higher simple pneumoconiosis during 35 years at various mean dust concentrations. (Data from Table I.)

■ ————— colliery mean data
 ○ ————— mean concentrations experienced by individuals

12 ordered X-ray classifications as a random process in discrete time units. Table II shows, for example, the frequencies of observed changes over 10 years among the 355 men listed in Table I as having experienced mean dust concentrations between 4.0 and 4.5 mg/m^3 during that period.

Table II. Matrix of transitions over 10 years for 355 coalface workers exposed to mean dust concentrations from 4.0 but less than 4.5 mg/m^3 .

INITIAL	RADIOLOGICAL CLASSIFICATION												Total
	0/-	0/0	0/1	1/0	1/1	1/2	2/1	2/2	2/3	3/2	3/3	3/4	
0/-	1	2											3
0/0		214	25	6	1		1						247
0/1			19	11	4	2	1	1					38
1/0				10	5	4	2	1	1				23
1/1				1	8	1	3						13
1/2						5	4	3		1			13
2/1							5	2	1				8
2/2								3	1	1			5
2/3									2				2
3/2										3			3
3/3													
3/4													
Total	1	216	44	38	18	12	16	10	5	5			355

If the numbers in each cell are divided by the corresponding row totals then the resulting array may be regarded as an estimate of a matrix of transition probabilities for the relevant time period. By hypothesis, particular transition probabilities are functions of dust exposure during the relevant transition period. The validity of the hypothesis

can be tested using observed data; strong evidence consistent with it, for ten-year periods, was produced by Jacobsen *et al* [1,7] and again by Jacobsen [9]. Assume now that for a given dust exposure during a period, transition probabilities are independent of earlier dust exposure. With this assumption estimates of transition probabilities for integral multiples of the observed time periods are possible by using a simple Markov-chain procedure. For a 20-year period the 10-year matrix is squared; for a 30-year period it is cubed, and so on. Again, if the assumption is valid, then transition probabilities relevant to half an observed time period can be estimated by finding a suitably structured matrix which when multiplied by itself gives a product equal to the original matrix.

4.3.2 Effect of the assumption

Statistical independence of radiological transition probabilities during consecutive periods with similar dust exposures is, at first sight, an unreasonable assumption for at least two reasons. On the one hand it can be argued that because radiological changes are associated with accumulation of dust in the lungs the probability of no transition during a second period is likely to be lower than in the preceding period; the dust accumulated, but not detected radiologically, during the first period will pre-dispose individuals to showing radiological changes on the classificatory scale during the second period. On the other hand it may be that some individuals are inherently less susceptible to the development of radiological changes than others. Probabilities of no change during the second period will then be higher than in the preceding period, since the hypothesized less susceptible individuals are more likely to constitute the group at risk during the second period. Notwithstanding these two objections, the assumption was made for the interim analysis. It was rationalized by appealing firstly to the substantial observed differences in risks of radiological change depending on the initial category. This factor presumably reflects the combined effects of the two opposite tendencies and possibly others. Given then that the data available covered a wide range of previous exposures it was thought likely that a simple Markov model would yield reasonable estimates of the probabilities required.

Subsequent examination of the results has confirmed that probabilities of no radiological change over a ten-year period for a

given dust exposure tend to decrease with increasing previous dust exposure. Table III for example shows results for sub-groups totalling 308 of the 355 men considered in Table II. It will be seen for instance that the percentages of men who showed no radiological change from the two lowest categories combined decreases from $68/77 = 88$ percent for men with less than ten years' previous exposure, to $42/53 = 79$ percent for men with previous exposures ranging from 20 to 30 years. The observed proportions progressing radiologically show the expected trend with increasing previous exposures, as do the prevalences in the three sets of starting categories. Similar trends were evident for other groups exposed to different concentrations of dust during the ten years.

In principle, extrapolation of results beyond ten years should be more reliable if differences depending on previous exposure are taken into account. Table IV shows the matrix product [A] obtained by successive multiplication of transition matrices corresponding to the three sub-groups defined in Table III. Also shown for comparison is [B], obtained by cubing the matrix corresponding to the pooled results from all 355 men (Table II). The latter calculation, which requires the approximation used for the interim analysis, is based on results from all men exposed to 4 to 4.5 mg/m^3 over ten years, including 47 men whose previous exposure to airborne dust exceeded 30 years. Using the simplified model [B], 4 of the 5 probabilities of no radiological change are lower than when previous exposures are taken into account. For this range of dust concentrations ten of the 15 possible probabilities of change were overestimated using the simplifying assumption. Analogous comparisons of results from men who experienced other ranges of dust concentrations during the ten years gave variable results (Table V). The example in Table IV concerning risks for men exposed to dust concentrations between 4 and 4.5 mg/m^3 is of particular interest because this concentration range corresponds to the maximum consistent with application of the current British coalmine dust standards.

5. Discussion

Serious problems of public health nowadays engender a continuous research effort, even if this work is conducted by different research groups rather than one. Opportunities for reviews of available scientific evidence concerning health hazards present themselves. Such opportunities should be taken.

Table III. Matrices of transitions over 10 years for 308 coalface workers exposed to mean dust concentrations from 4.0 but less than 4.5 mg/m³; by years of previous exposure to dust.

INITIAL STATE	FINAL STATE						Years of previous exposure to dust:	
	0/-&0/0	0/1	1/0	1/1	1/2	2/1+	Total	%
0/-&0/0	68	7	1	1			77	98
0/1								
1/0								less than 10;
1/1				1		1	2	2
1/2								
2/1+								
Total							79	100
0/-&0/0	92	6	3				101	78
0/1		7	3	2	1		13	10
1/0			3			3	6	5
1/1				2			2	2
1/2					2	2	4	3
2/1+						3	3	2
Total							129	100
0/-&0/0	42	8	2			1	53	53
0/1		7	5	2		2	16	16
1/0			4	4	1	1	10	10
1/1				5	1		6	6
1/2					2	3	5	5
2/1+						10	10	10
Total							100	100

Table IV. Estimated transition matrices for a 30-year exposure to dust concentrations from 4.0 but less than 4.5 mg/m^3

A : obtained from the product of matrices based on data in Table III

B : obtained by cubing the matrix based on data in Table II.

$$[A] = \begin{bmatrix} .6375 & .1940 & .0866 & .0210 & .0116 & .0493 \\ & .2356 & .2572 & .0962 & .0337 & .3774 \\ & & .2000 & .2000 & .0500 & .5500 \\ & & & .4167 & .0833 & .5000 \\ & & & & .2000 & .8000 \\ & & & & & 1 \end{bmatrix}$$

$$[B] = \begin{bmatrix} .6540 & .1437 & .0839 & .0457 & .0231 & .0496 \\ & .1250 & .1900 & .2156 & .1151 & .3543 \\ & & .0822 & .2107 & .1130 & .5941 \\ & & & .3318 & .0687 & .5995 \\ & & & & .0569 & .9431 \\ & & & & & 1 \end{bmatrix}$$

$$[A] - [B] = \begin{bmatrix} -.0165 & .0503 & .0027 & -.0247 & -.0115 & -.0003 \\ & .1106 & .0672 & -.1194 & -.0814 & .0231 \\ & & .1178 & -.0107 & -.0630 & -.0441 \\ & & & .0849 & .0146 & -.0995 \\ & & & & .1431 & -.1431 \\ & & & & & 0 \end{bmatrix}$$

A major lesson to be learnt from the results reported is that inferences based on grouped summaries of environmental data may give general guidance on the form of a dose-response relationship, but quantitative estimates may be biased. Careful examination may indicate the direction in which the bias is likely to operate. In the present case the indications were that the effect of the bias would be to overestimate rather than underestimate risks to health. The error incurred due to use of the simplifying assumption to extrapolate results is relatively small. Cubing a matrix which represents a weighted average of three sub-matrices (and one other) gave, as expected, a fairly good approximation to the product of the three sub-matrices. Moreover, the approximate transition matrices were based on larger numbers of observations, and therefore gave estimates of transition probabilities with relatively lower variances. This is reflected in the better correlation of these probabilities with increasing dust concentrations (Table V).

Diagonals of both [A] and [B] in Table IV demonstrate higher probabilities of further radiological change for men who begin a period with X-rays classified in categories other than the two lowest. The phenomenon was noted in earlier analyses (Jacobsen et al [1]; Jacobsen [9]) and is now confirmed. It has been suggested by Oldham [11] and Rossiter [12] that the higher risks for men with pneumoconiosis initially may be due entirely to the nature of the scale of radiological abnormality; no more sophisticated hypothesis is required to explain the observed results. This argument in no way diminishes the practical importance of the observation. So long as the 12-point scale is used to record radiological abnormality, so long can classification into categories other than the lowest be regarded as an index of increased risk. A dust standard designed to restrict long-term risks for new entrants to the industry with no pneumoconiosis will demonstrably be associated with much higher risks for older men who already show some early signs of the disease. The National Coal Board's regular X-ray surveys of all British miners [13] thus automatically constitute a medical screening programme; this supplements routine dust sampling designed to ensure compliance with the standard.

Table V. Estimates of probabilities of developing category 2 or higher simple pneumoconiosis during 30 years' exposure to various dust concentrations

- a. by simple Markov chain calculation
b. using information on previous exposure to dust.

Range of dust concentration (mg/m ³)	a. Simple Markov chain		b. Initial state augmented by years' previous exposures to dust			
	N	Mean dust concentration (mg/m ³)	Probability Estimates		Mean dust concentration (mg/m ³)	N
			a.	b.		
0.5-1.5	348	1.10	.0000	.0000	1.12	266
-2.0	427	1.72	.0000	.0000	1.72	336
-2.5	510	2.21	.0050	.0000	2.21	417
-3.0	430	2.68	.0087	.0000	2.68	351
-3.5	301	3.20	.0195	.0354	3.21	254
-4.0	350	3.70	.0236	.0078	3.71	307
-4.5	355	4.18	.0496	.0493	4.17	308
-5.0	291	4.71	.0331	.0243	4.71	257
-5.5	243	5.19	.0254	.0091	5.19	213
-6.5	335	5.91	.0220	.0000	5.91	291
-7.5	227	6.95	.0256	.0675	6.95	198
≥7.5	305	9.47	.1141	.1552	9.49	281
Total	4122					3479

N = number of men whose results over 10 years contributed to probability estimates

Acknowledgements

I am grateful to the many researchers who have conducted this project during the last 22 years and to the miners who volunteered their co-operation. Special thanks are due to my colleagues at the Institute of Occupational Medicine, particularly Mr. M.D. Attfield, and to the Chief Medical Officer of the National Coal Board, Dr. J.S. McLintock, for permission to publish. Dr. J.M. Rogan, Director of the research from its inception till 1973, saw the potentialities and difficulties associated with analysis of incomplete epidemiological data. He initiated the interim study and guided it to its conclusion. Opinions expressed in this paper are mine.

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DISCUSSION

SCHLIPKÖTER (Federal Republic of Germany)

Your country's 10-year programme was very carefully planned and carried out with precision. You found a correlation between dust amounts and pneumoconiosis frequency. Could you answer the following three questions?

1. Did you find that the starting age of the workers had any significance?
2. Did you find a high dust concentration effect (dust peaks) in the first years of employment?
3. Did you find that quartz concentration and mines waste were of importance in the development of pneumoconiosis?

JACOBSEN (U.K.)

1. In so far as age at survey or starting age are reflections of lengths of previous exposures, there is an effect, as is demonstrated in Table III of the paper. We have no evidence of any independent biological ageing effect on the radiological results.

2. We have not studied our data systematically for a possible "peak concentration" effect. Reisner (1971) has reported such an effect among coalminers in the Ruhr, although this was relatively small compared with the effect of cumulative dust exposure. Rogan et al (1973) have reported an interaction between age and dust exposure on pulmonary function (FEV₁₀) among the same cohort of miners considered in my paper, and this interaction is consistent with Reisner's observation.
3. We are currently analysing our data to determine whether and to what extent the quartz content of the dust affected results.

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STOPPS (Canada)

Were particle size distribution measurements of the coal dust in the various mines made? What was the relationship between the particle size and the gravimetric measurements?

JACOBSEN (U.K.)

Particle size measurements were made on dust samples collected during the first 10-year periods of observation. The concentrations of airborne dust from these samples had been expressed as the number of particles in the size-range 1 - 5 $\mu\text{g}/\text{m}$ of sampled air. Unfortunately, as reported by Rogan et al (1961), attempts to use estimated parameters from the observed particle size distributions in order to derive corresponding mass concentrations were not successful. This is why a series of field trials were conducted to determine experimentally the relationship between particle-count concentrations and mass concentrations in each of the 24 collieries involved in the study (reference (2) in the paper).

Reference

- ROGAN, J.M., RAE, S. and WALTON, W.H. (1967) in Inhaled Particles and Vapours II, Ed: C.N. Davies, pp. 493 - 508. Pergamon, Oxford, England.

VALUTAZIONE DELL'INQUINAMENTO DA RUMORE PRODOTTO DA UNA CENTRALE TERMoeLETTRICA SU DI UN QUARTIERE

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RIASSUNTO

Lo scopo dell'indagine è stato quello di valutare il disturbo arrecato dalla trasmissione del rumore e delle vibrazioni meccaniche di una centrale termoelettrica sugli abitanti di un quartiere della Riviera Ligure. E' stata condotta un'indagine oggettiva attraverso la misurazione diretta del rumore e delle vibrazioni a centrale termoelettrica ferma e in funzione, nonché un'indagine "soggettiva" mediante un questionario delle opinioni della popolazione del quartiere. Per garantire un elevato numero di risposte è stato utilizzato un questionario "mirato" e "partecipato".

Sono stati recapitati a domicilio e consegnati a ciascun abitante del quartiere di età pari o superiore a 18 anni 358 questionari che sono stati totalmente compilati e quindi utilizzati ai fini statistici. I questionari, opportunamente codificati, sono stati elaborati mediante il calcolatore elettronico.

La rumorosità misurata di notte all'interno di 6 abitazioni diverse, con le finestre aperte oscillava tra 43 e 32 dBA con la centrale termoelettrica ferma e tra 48,5 e 52 dBA con la centrale in funzione. Le vibrazioni misurate sulla zona centrale di un vetro di una finestra chiusa hanno presentato un massimo di ampiezza per le frequenze comprese fra i 12 e 30 Hz. I risultati della elaborazione statistica delle risposte del questionario hanno permesso di concludere che il rumore e le

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vibrazioni della centrale termoelettrica rappresentano per gli abitanti del quartiere una fonte di disturbo talmente grave da poter essere definita "intollerabile".

Gli autori sottolineano l'importanza del questionario quale strumento per la raccolta della soggettività e per la valutazione del grado di disturbo provocato da rumore.

ABSTRACT

The aim of the survey was to assess the effects of noise and mechanical vibrations produced by a thermal generating station on the inhabitants of a district in the Riviera Ligure region. Apart from conducting an objective survey consisting of direct measurements of noise and vibrations at the thermal generating station under operational and non-operational conditions, a "subjective" survey was carried out on the basis of a questionnaire on the opinions of the surrounding inhabitants. In order to ensure a large number of responses, an "active" and "passive" questionnaire was used.

Three hundred and fifty-eight questionnaires were completed by means of a door to door survey of all inhabitants over 18 years of age in the neighbourhood and were then used for statistical purposes. After proper coding, these questionnaires were processed by computer.

The noise measured at night inside six different types of home with the windows open varied between 43 and 52 dBA when the generating station was not operating and between 48.5 and 53 dBA when it was. The vibrations measured at the centre of closed window panes were found to be most intense for frequencies from 12 to 30 Hz. Statistical processing of the replies contained in the completed questionnaires led to the conclusion that the noise and vibrations from the generating station were so disturbing to the inhabitants of the district as to be considered "intolerable".

The authors consider the survey emphasizes the significance of questionnaires as a means of collecting subjective opinions so as to assess the degree of disturbance caused by environmental pollutants, among which noise is certainly to be included.

1. Introduzione

Nella vastissima letteratura che tratta della tollerabilità del rumore c'è ormai accordo quasi unanime sul fatto che la valutazione del disturbo da rumore non debba prescindere dal giudizio della popolazione interessata (Cederlof e coll., 1963; Noise final Report, 1963; Robinson e coll., 1963; Bolt e coll., 1964; Bishop, 1966; Kryter e coll., 1969). Nonostante questo accordo unanime, le norme e le leggi attualmente esistenti che stabiliscono i livelli massimi di rumorosità tollerabili senza fastidio non sono univoche. In Italia, in particolare, la normativa in questo campo è particolarmente carente, ed estremamente esigue sono le indagini condotte sulla popolazione per stabilire il quadro di disturbo corrispondente ai vari livelli di rumorosità in diverse situazioni. Per questo motivo, è stata condotta un'indagine sulla popolazione di un quartiere disturbato dal rumore e dalle vibrazioni prodotte da una centrale termoelettrica (C.T.E.) costruita nelle immediate vicinanze delle abitazioni.

2. Metodi

Il quartiere presso il quale è stata svolta la nostra indagine è composto da circa 20 caseggiati di 3-4 piani ciascuno, situato alla periferia di un piccolo comune della Riviera Ligure e confinante, da un lato, con la restante parte del paese e, dall'altro, con una centrale termoelettrica ivi insediata da 4 anni (vedi Fig. 1).

Una strada e un muro di circa 4 metri dividono il quartiere dalla centrale termoelettrica che occupa una zona in precedenza costituita per la maggior parte da prato. Il quartiere è abitato da circa 400 persone, rappresentate da impiegati, operai, piccoli commercianti, marittimi. Una percentuale irrilevante degli abitanti lavora presso la centrale termoelettrica. Gli appartamenti sono parte di proprietà, parte in affitto e parte a riscatto. La costruzione, l'acquisto, o comunque l'occupazione di queste abitazioni ha preceduto di alcuni anni il sorgere della centrale nella zona confinante.

Altri insediamenti industriali, costituiti da 3 fabbriche, si trovano a circa un chilometro di distanza in linea d'aria: pertanto, prima dell'insediamento della centrale, questa area poteva essere considerata come una zona "residenziale", mentre ora è stata trasformata in zona "semi-industriale" o "mista".

Al fine di stabilire il grado di disturbo provocato dal rumore della centrale termoelettrica, è stata svolta una duplice indagine: soggettiva, raccogliendo mediante un questionario le opinioni di tutta la popolazione del quartiere, e oggettiva, misurando direttamente il rumore e le vibrazioni nelle abitazioni.

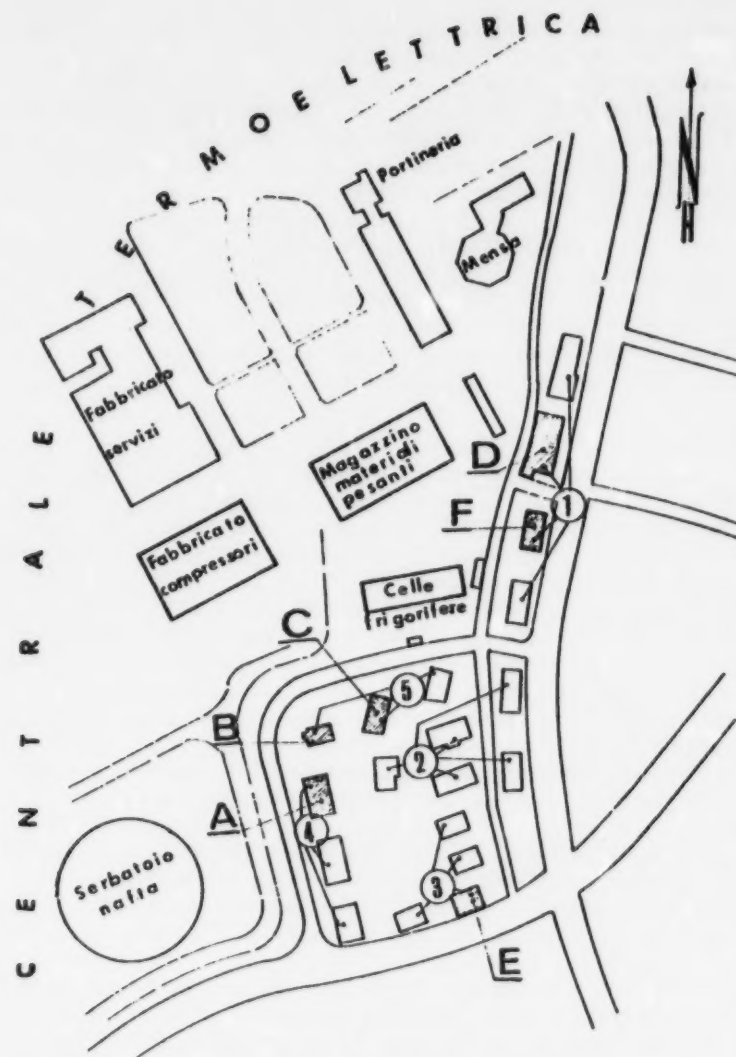


FIGURA 1 - Planimetria del quartiere dove è stata svolta l'indagine. Le lettere dell'alfabeto indicano i punti dove sono state effettuate le misure fonometriche. I numeri indicano le zone in cui è stato suddiviso il quartiere.

2.1. Il Questionario

E' stato utilizzato un questionario "mirato" e "partecipato" secondo una metodica originale alla cui preparazione abbiamo collaborato nel corso di precedenti indagini (Barlassina, 1972; Picotti, 1972; Grieco e coll., 1973). Secondo questa metodica è stata preparata una bozza di questionario, successivamente presentata e discussa nel corso di due riunioni con un gruppo di rappresentanti del quartiere e quindi in una ulteriore riunione collettiva con tutta la popolazione della zona interessata. La forma definitiva del questionario arricchita e verificata seguendo il metodo sopra esposto e recante una serie di istruzioni rivolte ai destinatari, è risultata composta da 44 domande, raggruppate in 4 sezioni.

La sezione I è dedicata a raccogliere notizie relative ai dati anagrafici del soggetto (nome e cognome esclusi) e alla collocazione della sua abitazione in rapporto con il quartiere e con la C.T.E. Le domande della II e III sezione sono rivolte ad evidenziare eventuali segni riferibili a disturbo da rumore o da vibrazioni, ad individuare la provenienza di tale rumore e/o vibrazioni nonché il grado di intensità. A questo scopo sono stati utilizzati riferimenti a condizioni reali analitiche che consentivano anche di stabilire vari livelli del disturbo. Per esempio, viene richiesto se il rumore sia tale da interferire con la conversazione, con la concentrazione e con il riposo notturno. Infine con la IV sezione viene indagata la presenza o meno di una sintomatologia patologica soggettiva connessa con alterazioni neuro-vegetative rapportabili verosimilmente al rumore e/o alle vibrazioni.

Una copia del questionario è stata consegnata ad ogni abitante del quartiere di età pari o superiore a 18 anni, e successivamente raccolta dopo la sua compilazione. In questo modo sono stati recapitati a domicilio complessivamente 358 questionari che sono stati totalmente utilizzati ai fini statistici.

Per la elaborazione dei dati del questionario, al fine di valutare la rilevanza della distanza della C.T.E. dal quartiere sul disturbo, è stato ritenuto opportuno suddividere il quartiere in 5 zone relativamente omogenee per numero di abitanti e differenti per distanza ed orientamento nei riguardi della C.T.E. Quindi si è proceduto a valutare la eventuale esistenza di differenze tra le zone e a determinare in quale delle 5 zone il disturbo da rumore e/o da vibrazioni e la morbidità soggettiva fossero maggiori rispetto alle altre mediante il calcolo dei parametri che seguono.

A) indice di disturbo da rumore (I.D.R.): questo indice, inteso come entità dell'interferenza del rumore con le normali attività fisiologiche e di relazione (conversazione, concentrazione, sonno) è stato calcolato sommando le risposte del questionario che inequivocabilmente confermano l'ipotesi di esistenza del disturbo. B) indice di disturbo da vibrazioni (I.D.V.): questo indice, inteso come valutazione soggettiva della presenza e della entità degli effetti delle vibrazioni sulle cose, è stato calcolato come il precedente sommando le risposte che confermano l'ipotesi di esistenza del disturbo da vibrazioni. C) indice di morbidità soggettiva (I.M.S.):

questo indice inteso come frequenza di sintomi patologici soggettivi, è stato calcolato sommando le risposte positive.

La elaborazione statistica dei dati è stata effettuata mediante i seguenti procedimenti. A) E' stata calcolata, ed espressa in valori percentuali la distribuzione delle frequenze e delle risposte per ciascuna delle domande del questionario. B) E' stata effettuata una serie di tabulazioni crociate delle variabili età, sesso e scolarità con le risposte alle domande relative ai tre indici di disturbo considerati. C) E' stato verificato se rispettivamente I.D.R., I.D.V., I.M.S. subiscano variazioni in rapporto con le 5 zone del quartiere in relazione con i piani di abitazione.

2.2. Misure fonometriche e vibrometriche

Le misure fonometriche e vibrometriche sono state effettuate dalla Sezione di Acustica Applicata dell'Istituto di Fisica Tecnica del Politecnico di Milano.

I rilievi di rumore, eseguiti di notte in alcune abitazioni del quartiere indicate nella piantina topografica (vedi Fig. 1), sono stati ripetuti tre volte: con la centrale termoelettrica ferma e le finestre aperte, con la centrale termoelettrica in funzione e le finestre rispettivamente aperte e chiuse. Sono stati usati: due misuratori di livello sonoro Brüel & Kjær tipo 2203 e 2204 dotati di capsule microfoniche Brüel & Kjær tipo 4131, registratore magnetico Nagra IV e uno Nagra III, un amplificatore Brüel & Kjær tipo 2606, un registratore di livello Brüel & Kjær tipo 2305 e un analizzatore di distribuzione statistica Brüel & Kjær tipo 4420. Le misure sono state eseguite tra la mezzanotte e le 3 di mattina, nell'aprile e giugno 1972, all'interno delle abitazioni prescelte, con il fonometro posto a circa 2 metri dalla finestra aperta e chiusa. In ciascuna postazione è stata fatta una registrazione magnetica dei segnali derivati dal fonometro, adattato in scala "lineare" previa incisione del segnale di livello sonoro campione. Successivamente, in laboratorio le registrazioni sono state filtrate in curva A e trascritte su carta, ricavandone allo stesso tempo la distribuzione statistica dei livelli sonori e lo spettro sonoro. Allo scopo di accertare la presenza di vibrazioni aeree immesse nel quartiere dalla centrale in funzione, sono stati eseguiti dei rilievi vibrometrici applicando un captatore accelerometrico sulla zona centrale della finestra chiusa. Il segnale elettrico derivato è stato inciso su un registratore a nastro magnetico a modulazione di frequenza. In fase di trascrizione, il nastro è stato riprodotto a velocità quadrupla di quella usata nella registrazione, e quindi analizzato con filtro selettivo e continuo. Sono stati usati un accelerometro Brüel & Kjær tipo 4330, un preamplificatore Brüel & Kjær tipo 2625, un registratore magnetico Brüel & Kjær tipo 7001, un amplificatore-analizzatore Brüel & Kjær tipo 2107, un registratore di livello Brüel & Kjær tipo 2305.

ZONA	I.D.R.	I.D.V.	I.M.S.
1	234 (62%)	124 (58%)	126 (55%)
2	185 (49%)	105 (48%)	87 (39%)
3	151 (63%)	64 (50%)	42 (37%)
4	271 (65%)	125 (55%)	88 (46%)
5	227 (76%)	100 (61%)	75 (50%)

TABELLA N° 1 - Valori degli indici di disturbo da rumore (I.D.R.), di disturbo da vibrazioni (I.D.V.) e di morbidità soggettiva (I.M.S.) corrispondenti a ciascuna delle 5 Zone del quartiere. Tra parentesi sono riportati i valori percentuali rispetto al numero totale delle risposte.

PIANI	I.D.R.	I.D.V.	I.M.S.
Terreno	83 (49%)	51 (47%)	24 (23%)
I°	237 (63%)	115 (55%)	96 (47%)
II°	258 (57%)	123 (53%)	105 (43%)
III°	288 (69%)	136 (59%)	114 (55%)
IV°	189 (68%)	84 (55%)	78 (54%)

TABELLA N° 2 - Valori degli indici di disturbo da rumore (I.D.R.), di disturbo da vibrazioni (I.D.V.) e di morbidità soggettiva (I.M.S.) corrispondenti a ciascuno dei 5 piani del quartiere. Tra parentesi sono riportati i valori percentuali rispetto al numero totale delle risposte.

3. Risultati

Per brevità non vengono riportati i dati analitici relativi a ciascuna delle 44 domande del questionario. Nelle tabelle 1, 2, 3, 4, 5 e 6 vengono riferiti i risultati più significativi ottenuti dalla elaborazione statistica del questionario.

Nella tabella numero 7 estrapolando e riassumendo dai grafici forniti dalla sezione di acustica applicata sono indicati i risultati delle misure fonometriche. Il rumore della centrale è di tipo continuo, costituito per la maggior parte da basse frequenze con un massimo di intensità fra i 50-200 Hz; è possibile distinguere un rumore di fondo che oscilla di $\pm 2,5$ dBA circa sul quale si inscrivono rari picchi di breve durata.

Per quanto concerne i rilievi vibrometrici, dagli spettrogrammi che sono stati ottenuti si può concludere per la presenza nella zona centrale di una finestra chiusa di vibrazioni che hanno il massimo di intensità compreso tra le frequenze di 12 e 30 Hz.

I valori dell'accelerazione non sono stati rilevati.

4. Discussione

L'esame dei risultati emersi dal questionario attraverso la valutazione della distribuzione delle frequenze delle risposte consente di stabilire se il rumore e le vibrazioni rappresentano un reale fastidio per la popolazione del quartiere. Tra le varie condizioni del quartiere ipotizzate come causa di disturbo (la carenza di mezzi di trasporto, il tipo di vicini, il rumore del traffico, il fumo e la polvere delle fabbriche, il rumore della C.T.E., il chiasso dei bambini, le vibrazioni della C.T.E., etc.), la rumorosità della centrale termoelettrica è indicata come la principale dal 65% della popolazione, mentre il 61% indica come tale le vibrazioni. Il 44% delle persone indica nel rumore e il 21% nelle vibrazioni provenienti dalla C.T.E. il fattore di disagio del quartiere sul quale vorrebbe intervenire prioritariamente. La somma di questi due valori supera largamente quella dei valori che si riferiscono a tutte le altre "cose da cambiare" considerate globalmente. Il rumore costringe il 28% della popolazione ad alzare la voce nella conversazione in casa, disturba la concentrazione del 46% dei soggetti, costringe l'86% a chiudere le finestre anche d'estate. Il 56% della popolazione stenta a prendere sonno e nel 39% dei casi la C.T.E. è indicata come la causa di ciò. Al 29% delle persone accade di essere svegliata improvvisamente di notte, nell'80% dei casi a causa del rumore della C.T.E., il 69% delle persone svegliate non riprende facilmente sonno. L'86% degli abitanti dichiara di percepire la esistenza nel proprio appartamento di vibrazioni e queste sono presenti nel 25% dei casi "sempre" e nel 34% "spesso". L'intensità delle vibrazioni è così elevata che il 15% dei soggetti riferisce di sentire vibrare il pavimento, il 16% nota spostamenti di oggetti, il 28% riferisce di danni sia pure modesti alle pareti e il 27% ai pavimenti. Il 61% della popolazione soffre di insonnia, il 69% di cefalea, l'87% di astenia mattutina, il 66% di inappetenza, il 65% è giudicato dai familiari o amici "una persona ner-

ZONE	I.D.R.		I.D.V.		I.M.S.	
	χ^2	g.d.l.	P	χ^2	g.d.l.	P
1-2-3-4-5	55,50	4	< 0,05	8,71	4	> 0,05
				17,96	4	< 0,05

TABELLA N° 3 - Valori di χ^2 , dei gradi di libertà (g.d.l.) e dei livelli di probabilità (P) per le 5 zone in rapporto a ciascuno dei 3 indici.

PIANI	I.D.R.		I.D.V.		I.M.S.	
	χ^2	g.d.l.	P	χ^2	g.d.l.	P
T-1-2-3-4	29,52	4	< 0,05	4,51	4	> 0,05
				35,49	4	< 0,05

TABELLA N° 4 - Valori di χ^2 , dei gradi di libertà (g.d.l.) e dei livelli di probabilità (P) per i 5 piani in rapporto a ciascuno dei 3 indici.

vosa". Nella grande maggioranza dei casi tali disturbi sono insorti negli ultimi 2-3 anni. E' risultato, inoltre, che le donne sono più disturbate degli uomini soprattutto per quanto riguarda il sonno, lo stesso vale per la classe di età intermedia (36-55 anni) e per coloro che dichiarano la più bassa scolarità. Dall'esame delle tabelle numero 1 e 3, in base ai valori degli indici I.D.R. e I.M.S. risulta che le zone più disturbate sono la 5, la 1 e la 4 rispetto alla 3 e alla 2. Per quanto riguarda l'I.D.V. non esistono differenze significative tra le varie zone; tuttavia le tabelle 5 e 6 indicano che le zone 1, 5 e 4 sono le più interessate dalle vibrazioni. L'esame della figura 1 dimostra che le zone più disturbate sono le più vicine alla C.T.E. Sono state messe in evidenza differenze significative anche tra i 5 piani di abitazione per gli indici I.D.R. e I.M.S. (vedi tab. 2 e 4) per cui risulta che gli abitanti del 3° e 4° piano sono più disturbati di quelli del 1°, 2° e del pianterreno. Questo fenomeno è verosimilmente in rapporto con l'azione protettiva verso il rumore esplicata dalle mura di cinta della C.T.E., che si frappongono tra questa e i piani di abitazione più bassi. Non sono state evidenziate differenze significative tra i piani di abitazione per quanto riguarda l'I.D.V.

I risultati e le considerazioni esposti permettono di affermare che il disturbo da rumore esiste inequivocabilmente, che la C.T.E. ne è di gran lunga la principale fonte responsabile, che le vibrazioni sono presenti in un gran numero di abitazioni, che esse costituiscono dopo il rumore la seconda causa di disturbo e che anch'esse provengono dalla C.T.E. I risultati ottenuti dal questionario concordano con quanto emerso dalle misure fonometriche. Infatti, anche con queste si dimostra che le misurazioni effettuate nel punto più lontano dalla C.T.E. hanno fornito i valori più bassi in termini di intensità del rumore, sebbene le differenze tra le zone non siano significative (vedi tab. 7). Ciò che invece risulta molto evidente è l'incremento di rumorosità riscontrato con l'entrata in funzione della C.T.E., che varia da un minimo di 8 dBA ad un massimo di 18 dBA. Per quanto riguarda la rumorosità nei diversi piani di abitazione, non è possibile stabilire un confronto in quanto le misurazioni non sono state effettuate in tutti i piani.

Le misure vibrometriche eseguite valgono soltanto a confermare l'esistenza delle vibrazioni denunciate dalla popolazione, e dimostrano che la loro massima intensità corrisponde a vibrazioni aventi una frequenza compresa fra 12 e 30 Hz. A questo proposito, giova ricordare che le vibrazioni a bassa frequenza (fino a circa 100 Hz) sono quelle capaci di provocare, a parità di accelerazione e spostamento, i maggiori effetti biologici, in quanto la frequenza di risonanza di numerosi organi ed apparati è compresa entro questi valori (Collana C.E.C.A. di Igiene e Medicina del Lavoro, 1967; Scherrer e coll., 1967; Odescalchi, 1972).

Non è possibile giudicare se le vibrazioni presenti nel quartiere siano dotate di una accelerazione tale da mettere in risonanza organi e apparati. Tuttavia, il fatto stesso che buona parte della popolazione ne percepisce la presenza induce a considerarle una fonte non trascurabile di disturbo.

ZONA	SI	NO	N.R.	TOTALE
1	62	29	9	(79)
2	25	55	20	(85)
3	29	44	27	(56)
4	46	49	5	(81)
5	55	40	5	(57)
				N = (358)

$$\chi^2 = 22,55$$

$$g.d.l. = 4$$

$$P < 0,05$$

TABELLA N° 5 - Domanda n° 30: Le vibrazioni hanno provocato secondo te, danni alle cose?

Percentuali delle risposte e delle non risposte (N.R.) date dai soggetti divisi in base alla zona di appartenenza. Tra parentesi il totale su cui è stata calcolata la percentuale.

ZONA	SEMPRE	SPESSO	QUALCHE VOLTA	N.R.	TOTALE
1	20	41	28	11	(79)
2	15	25	47	13	(85)
3	13	27	37	23	(56)
4	30	40	21	9	(81)
5	51	33	7	9	(57)
					N = (358)

$$\chi^2 = 49,41$$

$$g.d.l.$$

$$P < 0,05$$

TABELLA N° 6 - Domanda n° 27: In caso affermativo, le vibrazioni sono presenti:

Percentuali delle risposte e delle non risposte (N.R.) date dai soggetti divisi in base alla zona di appartenenza. Tra parentesi il totale su cui è stata calcolata la percentuale.

LUOGO DELLA MISURAZIONE	CENTRALE TERMoeLETTRICA FERMA FINESTRE APERTE	CENTRALE TERMoeLETTRICA IN FUNZIONE	
		FINESTRE APERTE	FINESTRE CHIUSE
A	39	49,5	38,5
B	40	48,5	39,0
C	35	52,0	-
D	40	51,0	35,0
E	27	48,0	32,0
F	33	50,0	33,0

TABELLA N° 7 - Rumorosità misurata nei 6 appartamenti prescelti, indicata come livello sonoro globale espresso in dBA, con centrale termoelettrica ferma e in funzione, con finestre delle abitazioni aperte e chiuse.

5. Conclusioni

Considerando globalmente le risposte alle domande del questionario è possibile affermare che il rumore e le vibrazioni della C.T.E. arrecano di sagio e disturbo a circa il 60-70% della popolazione del quartiere.

Questa percentuale così elevata indica chiaramente che il livello di rumorosità presente è superiore alla tollerabilità della popolazione e che per tanto deve essere considerato inaccettabile.

Questa conclusione alla quale siamo giunti dimostra l'importanza fondamentale dell'uso del questionario ogni qualvolta si debba giudicare del disturbo arrecato da un inquinante ambientale che, come il rumore, alteri lo stato di benessere soggettivo senza determinare modificazioni oggettive facilmente obiettivabili. Eseguendo unicamente delle misure fonometriche e confrontandone i risultati con una delle norme o raccomandazioni che regolano questa materia, avremmo ottenuto dei risultati piuttosto incerti o imprecisi.

Per esempio, con l'applicazione della Norma ISO 1996 che è la più usata in Italia, è possibile giungere ad indicare come livello di rumorosità ottimale per il quartiere un valore compreso tra 25 e 50 dBA, a causa delle diverse possibilità di scelta fornite da questa norma. Avremmo potuto, per tanto, dare dei giudizi estremamente contrastanti, non potendo basare la nostra scelta su dei dati concreti. D'altro lato, non riteniamo che la stessa Norma possa essere usata indifferentemente per valutare rumori con caratteristiche così diverse quali, per esempio, il rumore del traffico urbano e quello di una centrale termoelettrica. Infatti, il primo è estremamente variabile nel tempo, mentre il secondo è persistente e duraturo per anni interi. Non è escluso che questo carattere di estrema persistenza, senza possibilità di soste, possa aumentare il grado di disturbo arrecato alla popolazione.

Sulla base di queste considerazioni riteniamo che l'uso del questionario sia di fondamentale importanza nella valutazione della tollerabilità dell'inquinamento da rumore e che costituisca l'unica garanzia affinché non vengano accettati arbitrariamente dai tecnici livelli di rumorosità che molto spesso rappresentano il risultato di un compromesso con una realtà che non si vuole modificare, piuttosto che la preoccupazione di salvaguardare la salute e il benessere della popolazione.

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MERCURY-SELENIUM ASSOCIATION IN PERSONS EXPOSED TO INORGANIC MERCURY

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ABSTRACT

For the last few years we have been measuring the distribution of mercury in organs obtained from autopsies of persons working in or living around the mercury mine of Idrija, Slovenia. These investigations revealed an unexpected distribution pattern with very high uptake by thyroid and pituitary glands (by a factor of a thousand) accompanied by a very long biological half life. Kidney, normally considered to be the prime accumulator, ranked only third behind these glands. So far we had eight cases of professionally exposed miners and there was no exception to this pattern. In eleven subjects of the general population of Idrija, there was a greater variability but thyroid, pituitary and kidney still showed a considerable increase in concentration as compared to nonexposed persons, with values near background to factors of about fifty. Tables presenting mercury concentrations for three population groups (professional, population, controls) for many additional organs are given. Negligible methylmercury concentrations have also been found.

1. Introduction

In spite of numerous animal studies, information on inorganic mercury accumulation in humans is very limited, as noted by Nordberg and Skerfving(1) in the recent compilation of Vostal and Friberg, and by Berlin(2). Over the last few years, we have been analysing mercury in human organs from persons working in, or living around the mercury mine at Idrija, Slovenija, and comparing them with controls of no known exposure. This is part of a general survey of the uptake and distribution of mercury in the biosphere around the mine which has included plants(3,4) and fungi(5), animals(6) and the aquatic life of the contaminated river Idrijca(4,6) and man(20). Since Parizek and co-workers have shown(7,8) that selenium compounds exert a detoxifying effect (or in certain circumstances, a potentiating effect) on the toxicity of mercury compounds, and recent analytical results by Ganther et al(9) on tuna and especially on marine mammals by Koeman et al(10) indicate a close interrelation between the natural concentrations of the two elements in these species, we have extended our studies to the occurrence of both elements in the organs of exposed persons. Additionally we have also determined the methylmercury contents of some organs from mercury miners and the Idrija population.

2. Experimental

2.1. Analysis

Total mercury was determined by neutron activation analysis using a quantitative volatilization separation of the ^{197}Hg activity(11). The volatilization technique as applied to total mercury analysis has been further developed(16) so that additionally selenium, as 120 day ^{75}Se , may also be quantitatively volatilized

simultaneously from the same sample and measured separately from mercury. Methylmercury was analysed by a new method(12) using conventional gas chromatographic detection but with an isothermal distillation of volatile methylmercury cyanide in a Conway cell, instead of the usual Westöo extraction procedure(13-15).

2.2. Sampling

With the exception of some thyroid tissue excised by surgery, all samples were autopsy material and thus, apart from the relatively small number of subjects we have been able to examine, there was the further disadvantage that little control could be exercised over their distribution in terms of age, exposure etc. Of the eight mine workers so far analysed, only one died while still employed at the mine, the others having been in retirement for periods of from two to sixteen years.

Samples, stored at -25°C , were analysed in most cases without any pretreatment to avoid contamination problems or volatilization losses, the latter being as especial hazard with both mercury and selenium analyses. While for the larger organs (liver, brain) this procedure can be criticised on the grounds of inhomogeneity, replicate analyses showed a surprisingly small variation, and also such errors do not affect the mercury to selenium ratio measured simultaneously from the same aliquot.

3. Results and Discussion

3.1. Mercury Distribution

The average distribution of mercury in the three groups, the highly exposed mine workers, the general population of Idrija and non-exposed controls, is shown in Table I.

Table I. Average Hg content with standard deviation of human organs in ppm fresh weight

G r o u p :	Thyroid	Pituitary	Kidney	Liver	Lung	Brain
Mine Workers	35.2 [±] 28.5 (8)	27.1 [±] 14.9 (7)	8.4 [±] 4.9 (8)	0.26 [±] 0.25 (8)	1.11 [±] 0.89 (5)	0.70 [±] 0.64 ^x (6)
Idrija Population	0.70 [±] 0.45 ⁺ (10)	0.46 [±] 0.54 (11)	0.66 [±] 1.13 (11)	0.107 [±] 0.059 (11)	0.127 [±] 0.100 (10)	0.038 [±] 0.045 ⁺ (9)
Non-Exposed Controls	0.030 [±] 0.037 (16)	0.040 [±] 0.026 (6)	0.16 [±] 0.18 (5)	0.030 [±] 0.017 (6)	-	0.0038 [±] 0.0033 (3)

Figures in parentheses refer to the number of subjects analysed.

⁺excluding P.M., ^xexcluding T.A.

Striking is the very high accumulation of mercury in the thyroid and pituitary glands in exposed persons, being a factor of about 100 greater than the population group and about 1000 over the control group. Previously, kidney has been considered to be the prime accumulating organ, but in all eight mine workers, it ranked only third behind thyroid and pituitary. As noted above, seven of them had been in retirement for periods ranging up to 16 years, but the pattern of distribution of mercury in the organs found in all seven and the other subject (see Table II) was quite similar, with only a somewhat higher value in the liver of the latter, as might be expected. Thus on the basis of the distribution being virtually invariant with time since cessation of exposure, it is clear that retention of mercury in the organs with highest levels, namely thyroid, pituitary, kidney and brain, is very strong indeed.

As regards accumulation in the thyroid, though there was some previously published evidence suggesting its accumulating ability, its magnitude in man does not seem to have been observed. Artagavayieta(19) used ^{197}Hg as a scanning agent for thyroid tumours in man. Also Suzuki et al(17) found significant uptake of mercury in the thyroid of rats and rabbits following a single injection of mercury compounds, particularly inorganic ones, though only short time periods were followed. We did not observe(18) very striking accumulation (50-100 ng/g fresh weight) in the thyroid of rabbits exposed for long periods to natural mercury contamination in Idrija. Investigation of mercury-rich thyroid(20) showed that little mercury was contained in extractable proteins, and there only in the highest molecular weight fraction. A small scale survey(21) of some other trace elements in thyroid did not reveal any other correlations. Obviously in order to see the effects of mercury accumulation in the thyroid, detailed clinical investigations would be required involving

Table II. Mercury content of human organs in ng/g,
fresh weight-basis

Subject	Thyroid	Pituitary	Kidney	Liver	Brain	Lung
<u>Group I - Hg mine workers</u>						
^x B.A., 56y (5)	41300	64300 ^x	5500	108	181	127
O.A., 62y (10)	21300		9430	120	1500	1580
P.A., 42y (0)	34500	53660	18530	791	791	614
L.F., 52y (2)	19250	18000	6660	184	1430	-
F.M., 60y (5), 17y	7800	14500	7510	360	160	-
J.V., 59y (5), 21y	29700	13800	5970	370		830
B.P., 71y (16) 33y	26500	23900	2320	37		-
T.A., 71y (16), 29y	101000	41100	11400	65		2400

	Blood	Muscle	Spleen	Heart	Pancreas	Testis	Adrenal	G.
B.A.	1.6	8.5	25		36	295	223	
O.A.	4.8	14.4	23	18	42	37	238	
P.A.	10.0		188	98	352	526		
L.F.	17.4	106						
F.M.	7.0							
J.V.	78							
B.P.	72							
T.A.	20							

^xage, years in retirement, years exposed to Hg, respectively.

Table II continued

Subject	Thyroid	Pituitary	Kidney	Liver	Brain	Lung
<u>Group II - Population of Idrija</u>						
G.V., 62y, m	730	315	202	124	39	44
K.F., 40y, m	958		79	63	15	244
B.M., 75y, f	676	163	316	131	24	168
Š.Ž., 43y, f	122	975	526	48	76	122
B.S., 19y, m	69	776	4000	184	21	42
P.M., 71y, f	14400	590	760	67	110	68
D.I., 0.3 y	26	20	610	85		66

	Blood	Muscle	Spleen	Heart	Pancreas	Testis	Adrenal	G.
G.V.	3.7			12.2	15.1	8.7		
K.F.	3.6	4.9	11.8		14.8			36.6
B.M.	8.5	17			13			20
Š.Ž.	4.2	10	20		17			21
B.S.		24						
P.M.	17							

thyroid function, measurements related to size and number of follicles and the statistical incidence of malfunctions in exposed subjects.

The rather high values found in brain confirm the data of Takahata(22) on two mercury mine workers. Great variation between different sections and again, of course, the extreme retention are noticeable; this is also illustrated in Table 5 below. Also two out of three miners showed rather high levels (0.3 and 0.5 ppm fresh weight) in the testes, in agreement with the slow rate of excretion found in animal experiments by Berlin(23).

3.2. Methylmercury

The main source of contamination for both miners and the Idrija population are mercury vapour and dusts. In addition to the high levels in soil (typically 50-500 ppm), the exhaust stack of the distillation plant discharges 20-30 kg of mercury daily to the Idrija atmosphere. We have examined some subjects from both groups to determine the proportion of mercury which is accumulated in the methyl form, in the case of kidney, liver and brain.

As shown in the Table III, the absolute amounts found from 3 to 30 ng/g fresh weight, in both groups are low and very similar. Expressed as a fraction of the total mercury, in the population group it nevertheless amounts to 20 % on average in the liver and 26 % in the brain. It can probably be concluded therefore, that in vivo methylation does not occur, but that the small amounts represent ingested foodstuffs containing methylmercury (fish, meat, eggs).

Table III. Total and methylmercury contents in human organs in ppm fresh weight

Subject	Kidney		Liver		Brain	
	Hg	MeHg	Hg	MeHg	Hg	MeHg
Exposed Group						
P.A.	18.5	0.026	0.79	0.022	0.79	0.009
L.F.	6.66	0.013	0.18	0.010	1.43	0.004
Idrija Population						
G.V.	0.20	0.006	0.12	0.014	0.039	0.009
K.F.	0.079	0.005	0.063	0.015	0.015	0.003
B.M.	0.32	0.019	0.13	0.028	0.024	0.010
Š.Ž.	0.53	0.010	0.048	0.014	0.076	0.026
B.S.	4.0	0.011	0.18	0.023	0.021	0.002

3.3. Mercury and Selenium

The results of the simultaneous analyses of mercury and selenium from the same organ sample are shown in Table IV.

A remarkable correlation is noticeable between the contents for the organs with the highest mercury values, namely thyroid, pituitary and kidney. The weight ratios of mercury to selenium approximate to the molar ratio (2.54) in these organs. The same is true for brain as shown in Table V.

The correlation in subject T.A. is found in different brain sections. Since selenium, as an essential element, seems always to be present at levels at or above 0.1 ppm, whereas mercury in non-exposed persons can fall to almost zero, a near molar ratio will only be observed with rather elevated mercury levels. However, even slightly elevated mercury levels seem to result in above normal selenium values.

Since we have not yet been able to analyse both

Table IV. Hg and Se in human organs in ppm fresh weight

Subject:	Hg	Thyroid Se	Hg/Se	Hg	Pituitary Se	Hg/Se	Hg	Kidney Se	Hg/Se	Hg	Liver Se
Group I - Mine Workers											
P.M. (m)	7.8	3.2	2.4	14.5	6.1	2.4	7.5	2.5	3.0	0.36	0.38
J.V. (m)	29.7	12.6	2.4	13.8	6.4	2.1	5.97	2.1	2.8	0.37	0.40
B.P. (m)	26.5	12.3	2.2	27.7	13.3	2.1	2.32	1.6	1.5	0.037	0.36
T.A. (m)	101	41.1	2.5	47.9	-	-	11.4	5.1	2.2	0.065	0.38
Group II - Idrija Population											
P.M. (f)	14.4	5.72	2.5	0.59	0.39	-	0.76	0.70	-	0.067	0.21
D.I. ^x	0.026	0.16	-	0.020	0.34	-	0.61	0.47	-	0.085	0.12
Group III - Controls											
D.J. (m)	0.039	0.79	-	0.057	0.45	-	0.37	0.82	-	0.039	0.19
K.H. (f)	0.0023	0.46	-	0.044	0.34	-	0.011	0.54	-	0.010	0.17
^x ₄ month infant F.M. exposed 17 years, 5 years in retirement J.V. exposed 21 years, 5 years in retirement B.P. exposed 33 years, 16 years in retirement T.A. exposed 29 years, 16 years in retirement P.M. aged 82, life-long Idrija resident (son a miner)											

selenium and mercury in a miner still exposed to mercury, we should strictly speak of the effect as a molar mercury-selenium retention ratio, though it would seem likely that it will also be observed in man as an accumulative effect. Koeman et al(10) observed the same molar ratio over more than two decades of mercury concentration in the livers of marine mammals. Here also the mercury was present predominantly in the inorganic form. In our case, it seems that both mercury and selenium are excreted from liver rather more rapidly than the other mercury accumulating organs, where very high levels are retained after up to 16 years. (It is interesting to note that, according to Iwata et al(23), Uzioka(24) in 1960 found high levels of selenium, as well as inorganic mercury, in fish, cats and humans polluted with methylmercury).

Table V. Hg and Se contents of human brain sections in ppm fresh weight

Sample	T.A.		Hg/Se	B.P.		P.M.	
	Hg	Se		Hg	Se	Hg	Se
Cerebellum	2.42 2.34	1.38 0.93	1.8 2.5	0.15	-		
Striatum & cortex	13.2 2.96	6.05 1.45	2.2 2.1			0.071	0.17
Thalamus	8.16	3.33	2.5				
Hypothalamus				0.10	0.17		
Substans.nigra				0.073	0.17	0.020	0.15
Occip.cortex				0.18	0.23	0.24	0.25
Mod.oblongata	2.66	1.15	2.3				

In attempting to explain this effect, the strong mercury-selenium linkage should be considered, and the protective effects demonstrated against mercury compounds by selenium administration(7,8,23). The correlation between mercury and selenium definitely is causal, as is confirmed in the Idrija case by our findings of normal levels of selenium in dusts and soils (ca. 1 ppm). One can suggest that the effect is a natural protective effect operating in conditions of higher exposure. A selenium supplemented diet might be indicated for workers exposed to high mercury levels(8). The detailed metabolic explanation must await extensive further investigations, and we hope that these analytical results will stimulate further research into this phenomenon, which is clearly of considerable importance in the toxicity of mercury.

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DISCUSSION

BRAMAN (U.S.A.)

What analytical method was used for methylmercury analysis of tissues?

BYRNE (Yugoslavia)

Full details are described in reference (12). In brief, an isothermal distillation of methylmercury cyanide, generated in situ in the tissue, was employed. The volatile product was trapped on a ring of cysteine impregnated paper in the outer compartment of a Conway dish. Following acidification and extraction into benzene, the usual gas chromatographic detection was used.

PFANNHAUSER (Austria)

Have you any indications which kind of proteins bind mercury? Is it conceivable that detoxification by selenium is based on a greater binding of Se to these proteins.

BYRNE (Yugoslavia)

It is generally considered that mercury is bound on the sulphur containing ligands of proteins. The molar Hg/Se ratio suggests that mercury is bound to selenium, but the nature of the attachment to the protein is uncertain.

CHAMBERS (Ireland)

I am not quite sure of the source of the material for the analysis of the metals in the organs. Were the organs taken biopsy specimens or were they post-mortem specimens? If the latter case is the source, have any comparisons been made with biopsy material?

BYRNE (Yugoslavia)

They were all post-mortem specimens with the exception of most of the thyroid samples in the control group. In the latter group of samples no differences were noted between biopsy and post-mortem samples.

de BRUIN (Netherlands)

Three points arise:

1. Was there any exogenous source of Se contamination present in your investigation, or did the interaction concern only an influence of naturally occurring Se upon the distribution of exogenous Hg in the human organs?
2. Is there any evidence of thyroid and or generalized endocrinal disturbance in people working in or living around the Hg mine?
3. Concerning the type of interaction Hg/Se; has Se a protective or rather synergistic effect upon Hg toxicity?

BYRNE (Yugoslavia)

1. As stated in the paper, selenium levels were found to be in the normal range for the natural environment.
2. Not to our knowledge, though this should be investigated.
3. The interaction of Se and Hg is complex and can be of either type, see for example, the work of Parizek and co-workers referred to in the text.

WEBER (Yugoslavia)

1. What is, in your opinion, the point of having the results of mercury analyses given with apparently high precision when the notion of fresh or wet weight of organs in general is a rather undefined concept?
2. Have you any idea why mercury is accumulated in the thyroid gland?

BYRNE (Yugoslavia)

1. If selenium is also simultaneously analysed in the same sample, precise values are necessary to give a precise ratio. In general high precision is unnecessary, though still meaningful if the water content is also measured.
2. We have postulated an association with iodine and its metabolic cycle in the body. The scheme, involving the thyroid and pituitary glands, is described in more detail in reference (20) of the paper.

HINE (U.S.A.)

1. Why did you not analyse Hg and Se in tissues with higher cysteine content such as the skin and hair?
2. Were the values expressed in ppm by weight or milliequivalents per mass?

BYRNE (Yugoslavia)

1. Because of the strong likelihood of external mercury contamination, we consider analyses of such samples to be unreliable. Also selenium containing shampoos are in common use.
2. All results are expressed as ppm or ng/g on a fresh weight basis.

CLEMENTE (Italy)

Was the blood concentration of Se measured? In fact the ratio of Hg/Se in blood can indicate whether the Hg/Se ratio of 2.5 is due to an accumulation or to particular retention of Se in man in the presence of Hg concentrations.

BYRNE (Yugoslavia)

Yes such measurements were made. For mercury the blood values were in the normal range because of the interval between cessation of exposure and measurement. We hope to measure the ratio for miners still exposed.

UNTERSUCHUNG DER WIRKUNGEN AUF DEN MENSCHEN
HUMAN EFFECTS STUDIES
ETUDES DES EFFETS SUR L'HOMME
STUDI DEGLI EFFETTI SULL'UOMO
ONDERZOEKINGEN NAAR EFFECTEN BIJ DE MENS

Panel

Vorsitzender - Chairman - Président - Presidente - Voorzitter

F.G. HUETER (U.S.A.)

METHOD FOR A EUROPEAN STUDY ON
POSSIBLE EFFECTS OF AIR POLLUTION IN CHILDREN

PH. BOURDEAU

on behalf of the Commission's Working Party of experts on epidemiology.

Commission of the European Communities, Directorate General for Research, Science and Education, Brussels, Belgium.

ABSTRACT

A coordinated epidemiological survey on the relationship between air pollution and incidence and prevalence of respiratory affections in children has been planned with the participation of about ten institutes in the Member States of the European Communities.

This broad participation will provide results from a very large number of observations obtained in a significant number of geographical areas categorised according to their air pollution characteristics.

This survey will be carried out by means of a questionnaire (on health and socio-economic status of children) administered by fieldworkers, of physical measurements (height, weight, ventilatory function) performed on children in the schools, and air pollution measurements, in particular SO_2 and suspended particulate matter.

The protocol for the survey has been developed by a Working Party of experts on epidemiology set up in 1973 to advise the C.E.C. on its Environmental Research Programme in this area.

A pilot study will be first undertaken on a limited number of children followed by the main study on 20,000-30,000 children.

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1. Introduction

Epidemiological surveys are essential for the understanding of the health effects of air pollution. Investigations on the relative influence of individual pollutants are particularly useful. Although it has been shown that air pollution influences incidence and prevalence of respiratory symptoms and disease, as well as levels of ventilatory function in children and adults, very little is known about the independent effects of individual pollutants such as for instance smoke and sulphur dioxide. Areas with very contrasting degree of air pollution will be chosen in the Member States of the European Communities, in which appropriate investigations may be carried out.

2. Purpose of investigation

To determine the influence of air pollutants on respiratory symptoms, respiratory disease and ventilatory function in school children.

3. Methods

3.1 This survey will require a questionnaire designed to determine the incidence of past respiratory disease and present respiratory symptoms. The questionnaire will also need to elicit details of social and occupational factors of the family that could influence the incidence and prevalence of respiratory symptoms and disease and the levels of ventilatory function, as well as to aid comparability. It should, therefore, contain questions concerning the child's health, (e.g. occurrence of cough and/or breathing difficulties) and the socio-economic status of the family (e.g. type of housing and type of work of parents).

The questionnaire will be completed by the fieldworkers interviewing the child's parents at school and/or at home. By preference the mother of the child should provide the answers.

3.2 In addition the following physical measurements on the individual child will have to be made: height, weight and ventilatory function. Instructions for such measurements as well as for the administration of the questionnaire will be given in a Manual to be used by the fieldworkers.

4. Areas

The sites for investigation (a total of 20-25 areas) should be chosen according to the type of pollution. They should be characterized by very contrasting levels of air pollutants, mainly SO_2 and suspended particulate matter. Rural and low-polluted urban areas should also be considered.

It would also be of interest to locate areas polluted by other substances (e.g. NO_x , NH_3 , photochemical oxidants, etc...).

The characterization of atmospheric pollution in the areas to be selected should be based on regular measurements performed over a period of at least three years. The concentrations of atmospheric pollutants should be determined through comparable methods in the frame of air monitoring programmes of regional networks.

The measurements could be completed during the implementation of the survey by means of monitoring instruments installed in the schools.

Because of the importance of climatic factors, meteorological observations, should also be made during the investigations (temperature, wind rose, relative humidity etc...)

It is essential that the selection of the areas where to conduct the epidemiological survey be made in cooperation with experts on air monitoring.

Potential contractors will have to provide information on air pollution measurements currently made in the proposed areas by means of an appropriate form. Instructions regarding the air pollution measurements to be carried out in the proposed areas and the results to be reported are contained in a separate protocol.

5. Population to be studied

In each area where the study is to take place, 1.000 - 1.500 school pupils aged six years or more, and less than eleven years at the time of the beginning of the survey should be the object of the investigations. Both sexes are to be included in about equal proportion.

6. Recruitment and training of personnel

The persons (fieldworkers) who will be in charge of the administration of the questionnaires and the execution of the physical measurements during the survey should be, by preference, recruited among nurses, or student nurses, and/or social workers.

Uniform training procedures should be established within each country for the recruited personnel.

In order to be quite certain that the measurements performed in different areas are comparable, only one team of fieldworkers should be responsible for the measurements in all the individual projects in a given country. It would be advisable to set up a joint training session for such responsible personnel from each country.

The administration of the questionnaire will be carried out by the two fieldworkers assigned to single areas.

The work of the teams in the various countries during the period of survey is to be supervised by at least two of the above mentioned responsible fieldworkers. They will re-measure, with the local team, a sample of the children in order to make certain that the results which have been obtained are comparable.

The work schedule to be established for the fieldworkers should include periods of: - training and familiarization

- interviews (administration of questionnaire)
- physical measurements
- refresher courses
- additional interviews and measurements (cases of dubious answers and incorrect results)

The number of weeks required for each period may vary from country to country according to qualifications of recruited personnel, working conditions and families and children responding promptness. Since variations in ventilatory function, symptoms, etc... occur according to season, as short a time as possible should be spent on field observations (physical measurements and interviews to fill in the questionnaires).

7. Data handling programme

7.1 Data collection

For each area : - gathering of the results of physical measurements (recorded on special forms) and filled questionnaires for each child

- report on air pollutants measurements performed by local air monitoring stations (including data for at least three years preceding the beginning of the survey) and/or by means of instruments installed in the schools
- report on meteorological observations made during the investigations (temperature, wind rose, relative humidity...)

7.2. Data analysis

The data from each area of each country, transferred locally on punch cards, are processed in a central place :

- analysis of questionnaire answers by age-sex-area categories
- analysis of results of lung function measurements by age-sex-area categories. Means, frequency distribution, s.d., s.e. etc...
- analysis of air pollution and meteorological data
- establishment of the relationship between air pollution characteristics and respiratory symptoms and disease in children.

PRESENTATION ET DISCUSSION DU PROTOCOLE D'UNE
ENQUETE EPIDEMIOLOGIQUE FRANCAISE SUR LES RELATIONS
ENTRE POLLUTION ATMOSPHERIQUE ET AFFECTIONS
RESPIRATOIRES CHRONIQUES

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Etude préparée avec les responsables de l'enquête dans les 8 centres:

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RESUME

A la demande du Ministère de la Protection de la Nature et de l'Environnement et en collaboration avec le Ministère de la Santé Publique et de la Sécurité Sociale, une étude épidémiologique sur les relations entre pollution atmosphérique moyenne et affections respiratoires chroniques ou à répétition, a été

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entreprise en France. Le protocole et les méthodes de travail ont été élaborés en commun par 7 équipes travaillant dans 8 centres.

28 zones de 1000 sujets environ ont été constituées (2 à 4 zones par centre) en tenant compte de plusieurs facteurs:

- importance de la pollution antérieurement connue en acidité forte (exprimée en SO_2) et en fumées noires, de façon à obtenir des zones aussi contrastées que possible. A ces mesures ont été ajoutées celles du dioxyde de soufre, d'oxydes d'azote, des poussières par gravimétrie.

- existence d'une population suffisante en fonction de critères choisis: catégories socio-professionnelles, âge, durée de résidence, nationalité.

Des renseignements sur l'état respiratoire des sujets, leurs antécédents, leur niveau de vie ... sont recueillis à l'aide d'un questionnaire et d'un examen spirométrique par des enquêteurs, à domicile.

Quelques points du protocole sont discutés et notamment la difficulté de trouver des populations socialement comparables habitant des zones peu étendues et fortement contrastées au point de vue pollution.

ABSTRACT

An epidemiological survey on the connection between mean atmospheric pollution levels and chronic or recurring respiratory ailments has been undertaken in France at the request of

the Ministry for the Protection of Nature and the Environment and the Ministry of Public Health and Social Security. The report and working methods were drawn up jointly by seven teams working in eight centres.

Several factors were considered in the choice of 28 zones of approximately 1000 test subjects (2 to 4 zones per centre):

- the extent of previously known pollution from strong acidity (expressed in SO_2) and black smoke so as to have zones which contrasted as far as possible. In addition, measurements for sulphur dioxide and nitrogen oxides were included, as well as gravimetical dust counts.

- presence of sufficient numbers of population corresponding to selected criteria: social and professional groups, age, length of residence, nationality.

Data on the test subjects' respiratory condition, past history, standard of living, etc. are collected by means of a questionnaire and a spirographic test carried out at the subject's home by research workers.

Certain aspects of the report are discussed, notably the difficulty in finding socially comparable population groups living in zones which are not too widespread but at the same time are strongly contrasted with regard to pollution levels.

1. INTRODUCTION

En 1973, à la demande du Ministère de la Protection de la Nature et de l'Environnement, en collaboration avec le Ministère de la Santé Publique et de la Sécurité Sociale, il a été décidé d'entreprendre une étude sur les relations entre la pollution atmosphérique moyenne et les affections respiratoires chroniques ou à répétition par la méthode épidémiologique.

Le principe de l'enquête est le suivant :

- choisir des zones dont la pollution est de type et de niveau moyen différent ;
- examiner sur le plan respiratoire (les voies respiratoires étant considérées comme un réacteur privilégié) des populations résidant dans ces zones.

Cette étude est conduite dans 8 centres (villes de Bordeaux, Lille, Lyon, Mantes, Marseille, Rouen, Toulouse et région de Fos).

Une telle étude se heurte à 3 types de difficultés :

- complexité du facteur pollution ;
- multiplicité des facteurs étiologiques des affections respiratoires ;
- mise au point d'un protocole commun et harmonisation des méthodes de travail de 7 équipes différentes.

Le protocole de cette enquête est présenté ici et certains points discutés.

2. LA POLLUTION

2.1 Choix des postes

Toutes les villes disposaient avant le début de l'enquête d'un réseau de mesure de l'acidité forte (exprimée en SO_2) et des fumées noires (postes "SF"). Les mesures faites en 1971 ont permis de déterminer des points aussi contrastés que possible en qualité et en quantité, permettant des comparaisons entre les différents centres et quelquefois dans un centre entre différentes zones (Bordeaux, Lyon, Marseille).

Les moyennes mensuelles se situaient entre 20 et $170 \mu\text{g}/\text{m}^3$ pour le SO_2 et entre 30 et 200 pour les fumées noires.

2.2 Choix des polluants

Pour essayer de préciser le facteur "pollution", il a été décidé

d'adjoindre aux mesures de l'acidité forte et des fumées noires considérées comme des "indices de pollution" des mesures du dioxyde de soufre par la méthode "Bourbon-Malboscq", des oxydes d'azote (NO , NO_2) par la méthode "Griess-Saltzman", des poussières par gravimétrie.

Les problèmes propres aux mesures, particulièrement ceux concernant leur harmonisation, feront l'objet d'une prochaine communication.

2.3 Représentativité des points de prélèvement

Il est difficile de dire dans quelle mesure la pollution déterminée aux points d'emplacement des postes est représentative de la pollution d'une zone. Tout au plus, peut-on affirmer que l'étendue des zones que l'on veut ainsi caractériser, doit être aussi limitée que possible. Il reste que les personnes habitant dans ces zones sont inégalement soumises à cette pollution : migrations quotidiennes, temps passé à l'intérieur des maisons ...

3. LA POPULATION

La population a été choisie en fonction de deux exigences :

- habiter à proximité de postes de mesure intéressants par leurs résultats ;
- avoir une certaine homogénéité sociale.

28 zones de 1000 sujets environ, présentant les critères d'admission à l'enquête, ont ainsi été constituées (2 à 4 zones par centre) à partir des données démographiques du recensement général de 1968 (INSEE).

La sélection des ménages, et à l'intérieur des ménages des sujets, nécessite un recensement exhaustif de la population pour lequel un questionnaire a été établi.

3.1 Critères de sélection des ménages

Les ménages sont sélectionnés en fonction du chef de ménage^o ; celui-ci doit être âgé de 25 à 59 ans, de nationalité française (pour éviter des difficultés linguistiques dans une enquête par questionnaire), résider dans la zone depuis 3 ans au moins (durée minimum pour pouvoir juger des effets d'une pollution moyenne). Le chef de ménage doit appartenir à l'une des catégories socio-professionnelles^o suivantes : "patrons

^oDéfinitions de l'Institut National de la Statistique et des Etudes Economiques (INSEE)

ENQUETE EPIDEMIOLOGIQUE COORDONNEE EN FRANCE

a) Nombre de sujets admis pour la pré-enquête

<u>Ménages</u> <u>visités :</u>	<u>" Admis à l'enquête "</u>	
	<u>Ménages</u>	<u>Sujets</u>
6 175	681 °	1 452 { 1 225 Adultes 227 Enfants

° N'étaient admis que les ménages dont le chef était ou cadre moyen ou employé (C.S.P. 4 ou 5 de l'INSEE).

b) Poids des différents critères dans l'élimination :

- <u>des ménages</u> :	• Nationalité du chef de ménage = 5 %
	• Ancienneté de résidence 3 ans = 20 %
	• C.S.P. du chef de ménage . . = 79 %
- <u>des sujets</u> :	• Age = 32 %

TABLEAU 1 : RESULTATS du RECENSEMENT de la POPULATION lors
de la PRE-ENQUETE dans CINQ CENTRES.

de l'industrie et du commerce", "professions libérales - cadres supérieurs", "cadres moyens - employés", "personnel de service".

3.2 Critères de sélection des sujets

L'étude porte sur les adultes des deux sexes, âgés de 25 à 59 ans et leurs enfant de 6 à 10 ans. Ces deux tranches d'âge constituent, séparément, des groupes relativement homogènes. De plus, les enfants de 6 à 10 ans, en grande majorité non fumeurs et scolarisés près du domicile, sont essentiellement soumis à la pollution atmosphérique de la zone étudiée.

3.3 Discussion du choix de la population

Le choix de la population est le seul point de protocole que les enseignements de la pré-enquête ont fortement marqué et qui mérite discussion.

Cette population n'est pas aussi homogène que souhaité. Initialement, il avait été prévu de ne retenir que deux catégories socio-professionnelles voisines : "cadres moyens" et "employés". Une zone de pré-enquête comportant 1000 ménages environ a été étudiée dans chaque centre. Là où l'INSEE avait recensé 1000 ménages dont 200 "cadres moyens - employés", comprenant 600 sujets, les critères de sélection propres à l'enquête (durée de résidence, âge, nationalité) n'ont permis de retenir que 100 ménages et 200 sujets en moyenne. Le tableau 1 montre les résultats du recensement des ménages obtenus lors de la pré-enquête conduite dans 5 centres. Le faible rendement est coûteux en temps et en argent et entraîne une extension de la surface de la zone.

Ces constatations ont conduit à élargir les catégories socio-professionnelles retenues; ceci introduit un facteur d'hétérogénéité qu'il faudra prendre en compte au moment de l'analyse.

Cependant, certaines catégories, comme les "ouvriers", n'ont pas été retenues car la pollution professionnelle est parfois bien supérieure à la pollution atmosphérique générale et, par sa diversité, aurait introduit un biais difficilement contrôlable sans une étude précise du lieu de travail (entreprise, poste de travail ...). D'autres catégories ont été éliminées car inexistantes en ville ("agriculteurs") ou très hétérogènes ("personnes non active", "autres catégories").

• Cadres moyens et Employés

.. " " " + Patrons de l'Industrie et du Commerce,
Cadres supérieurs et Professions libérales, Personnels de service.

- sont exclus : les Ouvriers, Agriculteurs. divers.

TABLEAU 2 : NOMBRE de SUJETS qui AURAIENT ETE ADMIS par ELARGISSEMENT des CATEGORIES SOCIO-PROFESSIONNELLES

Avec les nouvelles catégories socio-professionnelles admises à l'enquête, les renseignements collectés lors de la pré-enquête montrent que pour 6 175 ménages visités, 1 204 auraient été admis, soit 2 621 sujets (tableau 2).

Cet élargissement permet de doubler, pour une même surface, le nombre de sujets ou pour un même nombre de sujets, de diminuer le rayon de la zone de 30%.

4. RECUEIL des DONNEES CONCERNANT les SUJETS ADMIS à l'ENQUETE

Les données concernant les sujets admis à l'enquête sont recueillies à domicile à l'aide d'un questionnaire et d'un examen spirométrique simple qui permettent d'obtenir des renseignements sur l'état respiratoire et sur les facteurs étiologiques à prendre en compte au moment de l'analyse.

4.1 Etat respiratoire du sujet

4.1.1 Un questionnaire dérivé du questionnaire CECA pour l'étude de la bronchite chronique et de l'emphysème pulmonaire est utilisé. En fonction des buts propres à l'étude, quelques questions ont été supprimées (ainsi une seule question est posée sur la dyspnée d'effort), d'autres ont été ajoutées, notamment sur les voies aériennes supérieures.

Un questionnaire du même type a été élaboré pour les enfants et doit être posé aux parents.

4.1.2 Un examen spirométrique simple est fait à chaque sujet à l'aide d'un spirographe à sec portatif (Vitalograph) qui permet de calculer sur un tracé d'expiration forcée, CV, VEMS, VEMS/CV, VEM 25-75 %.

4.2 Facteurs étiologiques à prendre en compte

Une partie du questionnaire permet de noter pour chaque sujet, l'âge, le sexe, les antécédents pathologiques, le tabagisme, l'histoire professionnelle, l'exposition professionnelle éventuelle, le niveau d'études, la durée de résidence dans la zone étudiée. Les questions sur l'histoire professionnelle ont été simplifiées à la suite de la pré-enquête.

Pour chaque ménage, quelques renseignements sur les conditions de logement sont relevés à l'aide d'un questionnaire permettant d'avoir une idée de la pollution intérieure éventuelle par le chauffage et de préciser le niveau social.

5. CONCLUSION

L'étude du protocole de l'enquête épidémiologique française sur les relations entre pollution atmosphérique moyenne et affections respiratoires chroniques est une illustration des difficultés de toute étude de ce type.

Le rôle probablement mineur de la pollution atmosphérique et, particulièrement de son taux moyen, dans la pathologie respiratoire exige pour être mis en évidence que l'étude se déroule dans des zones fortement contrastées. La multiplicité des facteurs étiologiques connus et inconnus entraîne des exigences parfois contradictoires. Le choix, pour cette enquête, a été difficile entre : étudier une population hétérogène mais groupée autour des points de mesure de la pollution, ou une population homogène, au point de vue social, mais alors dispersée.

Une pré-enquête a été menée pour tester le protocole et les méthodes. Elle a montré la nécessité d'élargir les catégories socio-professionnelles et d'intensifier l'harmonisation des méthodes par une étude de comparabilité à tous les niveaux : mesures chimiques, questionnaires, examens spirométriques.

Etude subventionnée par le Ministère de la Protection de la Nature et de l'Environnement et par le Ministère de la Santé Publique et de la Sécurité Sociale.

ÜBER VERÄNDERUNGEN EINIGER BIOLOGISCHER PARAMETER BEI SCHULKINDERN IN GEBIETEN MIT UNTERSCHIEDLICH STARKER LUFTVERUNREINIGUNG

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KURZFASSUNG

Die vergleichende Untersuchung von Bevölkerungskollektiven in stark luftverunreinigten Gebieten und in Gegenden mit relativ sauberer Aussenluft ist eine der Möglichkeiten, den Einfluss der Luftverschmutzung auf den Gesundheitszustand des Menschen zu erforschen. Im Rahmen einer solchen epidemiologischen Studie wurden von uns in den Jahren 1968-74 Kindergruppen in der CSSR, der BRD und der DDR untersucht. Gegenüber den in den Kontrollregionen lebenden Kindern wurde hierbei in den exponierten Kollektiven wiederholt ein häufigeres Vorkommen vergrößerter und zerklüfteter Gaumenmandeln sowie vergrößerter regionärer Lymphknoten beobachtet. Die Zahl pathogener Keime auf den Tonsillen war hier höher, der Muramidasespiegel im Speichel niedriger als bei den Kontrollen. Die Kinder in den luftverunreinigten Arealen zeigten regelmässig eine relative Verspätung der Knochenreifung und eine relativ erhöhte Erythrozytenkonzentration; ferner fanden wir den mittleren Hämoglobingehalt und die Chemoresistenz der roten Blutkörperchen verändert. Der von uns positiv geführte internationale Vergleich beweist die Allgemeingültigkeit dieser Ergebnisse.

ABSTRACT

The comparative study of population groups in areas of high air pollution and in districts with relatively clean ambient air is one method of investigating the influence of air pollution on human health. As part of an epidemiological study of this kind we examined groups of children in the CSSR, the BRD and the DDR from 1968 to 1974. It was repeatedly noted that enlarged and fissured tonsils as well as enlarged regional lymph nodes occurred more frequently among the exposed groups than among the children living in the control areas. The number of pathogenic germs on the tonsils was higher and the muramidase level in the saliva was lower than among the control groups. The children in the air polluted areas were regularly relatively late in reaching bone maturity and had a relatively high erythrocyte count; further, we found changes in the average haemoglobin value and the chemoresistance of the erythrocytes. The international comparison conducted by us proves the general validity of these results.

Einführung

Eine Möglichkeit, die Auswirkungen der atmosphärischen Verunreinigung auf die menschliche Gesundheit zu erfassen, ist die vergleichende Untersuchung von Bevölkerungskollektiven, die in luftverschmutzten bzw. relativ luftreinen Gebieten unter im übrigen möglichst ähnlichen Bedingungen leben. Als besonders geeignet hierfür betrachten wir in Übereinstimmung mit Kapalín (1) und Symon (2) die 7-12jährigen. Denn in diesem Alter sind die uns interessierenden Entwicklungsparameter von der Pubertät noch unbeeinflusst, und wir können in dieser Altersstufe eine schnellere und intensivere Reaktion auf Umweltreize erwarten als beim Erwachsenen, ohne fürchten zu müssen, daß die Abwehrmechanismen noch nicht voll entwickelt sind oder die Expositionsdauer unzureichend ist.

Studienplan

Für unsere Untersuchungen des biologischen Status von Schulkindern haben wir die Regionen mit unterschiedlich starker Luftverunreinigung aufgrund der Angaben und nach den Empfehlungen der in der ČSSR, der BRD und der DDR für die Immissionsüberwachung zuständigen Gremien ausgewählt. In den einzelnen Untersuchungsräumen dieser drei Staaten wurden Kollektive mit einem mittleren Alter von rund 10 Jahren aufgestellt, die beide Geschlechter in etwa gleichem Anteil umfaßten; insgesamt haben wir von 1968 bis heute ca 4500 Kinder untersucht. Bei den meisten unserer Feldstudien wurden vor der eigentlichen Untersuchung Fragebogenaktionen durchgeführt, teilweise auch die Eltern direkt interviewt, wobei wir der Expositionsdauer des Kindes, den von ihm durchgemachten Erkrankungen, seiner Ernährungsweise und den sozio-ökonomischen Verhältnissen der Familie besondere Beachtung schenkten. Diese anamnestischen Daten wurden, soweit möglich, zum Zeitpunkt der klinischen, somatometrischen und Labor-Untersuchung jedes Kindes überprüft und ggf. ergänzt. In die Endauswertung nahmen wir nur die Daten jener Kinder hinein, die nach Anamnese und klinischer Beurteilung als gesund zu bezeichnen waren.

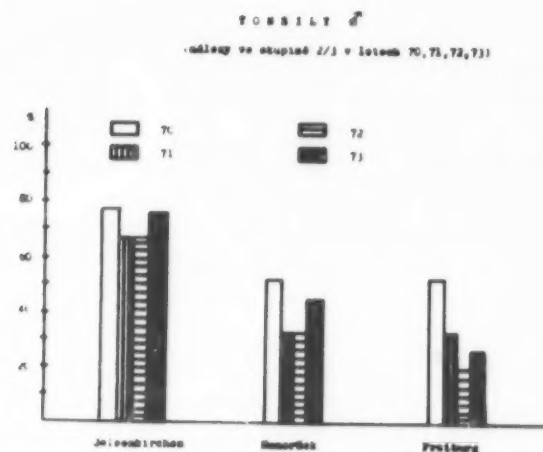


Abb. 1. Tonsillenbefund "mäßig bis stark verändert" (2/3) der Knaben; Häufigkeitsprozentwerte von 4 Jahren aus Gelsenkirchen (expon.) sowie den Räumen Hunsrück und Freiburg (Kontrolle)

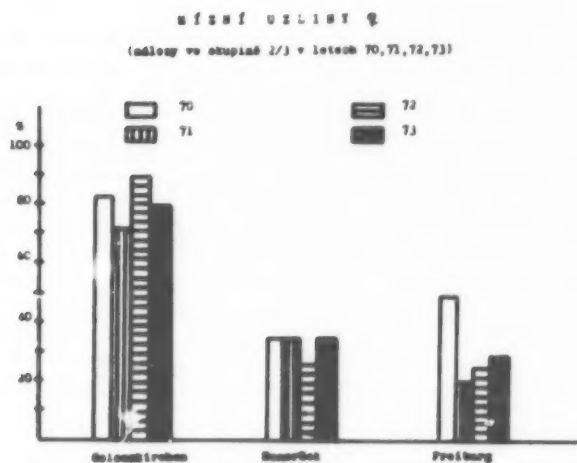


Abb. 2. Lymphknotenbefund "mäßig bis stark verändert" (2/3) der Mädchen; Häufigkeitsprozentwerte von 4 Jahren aus Gelsenkirchen (expon.) sowie den Räumen Hunsrück und Freiburg (Kontrolle)

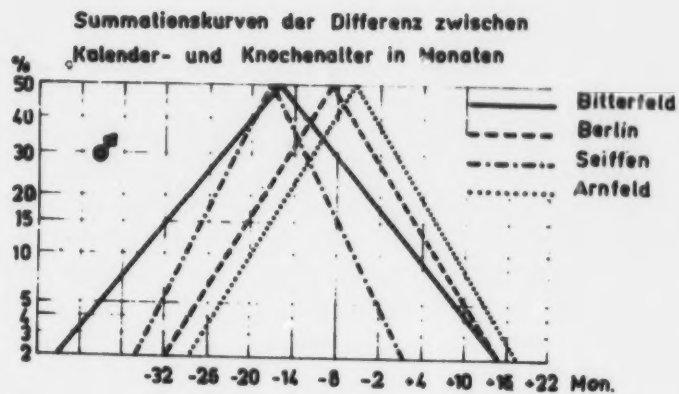


Abb. 3. Wert "Knochenalter minus Kalenderalter" (Monate) der Knaben; Summenhäufigkeiten für Bitterfeld und Seiffen (expon.) sowie Arnfeld und Berlin (Kontrolle)

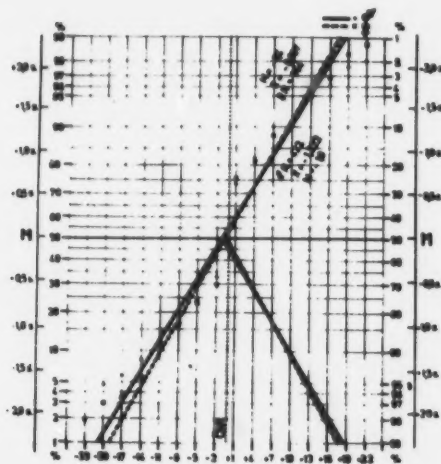


Abb. 4. Knochenreifungszustand der deutschen Population, bezogen auf die tschechischen Standardwerte; Summenhäufigkeit

Studienergebnisse

Die Befunde der Kinder, die städtisch-industriellen Luftverunreinigungen unterschiedlicher Stärke exponiert waren, lassen beim Vergleich mit den Kontrollbefunden für die Mehrzahl der diagnostischen Parameter Unterschiede erkennen (Dolgener, 3; Schmidt, 4). Die beobachteten Veränderungen bewegen sich meist in der physiologischen Schwankungsbreite; die Unterschiede zwischen den belasteten Gruppen einerseits und den Kontrollkollektiven andererseits sind dennoch fast immer statistisch signifikant. Einige dieser Veränderungen konnte Schmidt (5) im Tierversuch reproduzieren und dadurch ihren Kausalzusammenhang mit Komponenten der Luftverunreinigung wahrscheinlich machen.

Im einzelnen fand man bei den exponierten Kindern stets relativ häufiger als bei den Kindern in den Reinluftgebieten vergrößerte und zerklüftete Gaumenmandeln (Abb. 1) und vergrößerte regionale Lymphknoten (Abb. 2). Diese Beobachtung haben wir bei allen unseren Aktionen in der ČSSR, der BRD und der DDR, und zwar wiederholt, gemacht. Die Kinder in den verunreinigten Gebieten erwiesen sich ferner regelmäßig in ihrer Knochenreifung gegenüber den Kontrollkindern als verspätet, was wir als ein Zeichen ihres relativ geringeren biologischen Alters verstehen müssen (Abb. 3). Der Ossifikationsgrad wurde von uns auf der Basis des tschechischen Standards bestimmt, dessen Anwendbarkeit nach vergleichenden Studien von Pelech (6) gegeben ist (Abb. 4). Weiterhin zeigten die Kinder in praktisch allen von uns untersuchten Belastungsgebieten eine höhere Erythrozytenkonzentration als die Kinder in den Reinluftarealen (Abb. 5). Entsprechend war bei generell einheitlichen Hämoglobinwerten der mittlere Hb-Gehalt des Erythrozyten (HbE) unter Expositionsbedingungen, wenn auch nicht immer eindeutig, relativ vermindert. Die Chemoresistenz der roten Blutkörperchen schließlich, bestimmt nach der Erythrogramm-Methode, fanden wir in den belasteten Kollektiven gegenüber den Kontrollgruppen sowohl erhöht als auch erniedrigt (Abb. 6). Die genannten Unterschiede bestehen bei Jungen und

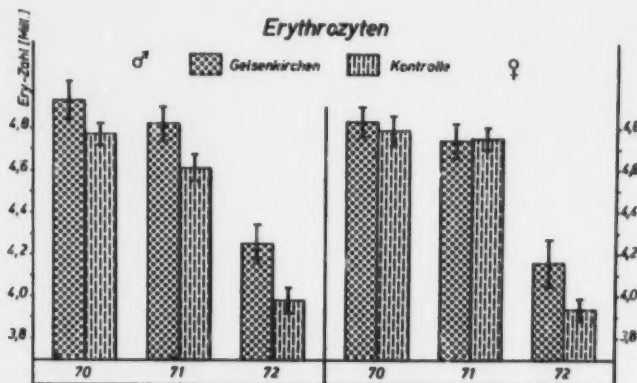


Abb. 5. Erythrozytenzahl (Mill./mm³); Mittelwerte mit Vertrauensbereich von 3 Jahren aus Gelsenkirchen (expon.) sowie den Räumen Hunsrück und Freiburg (Kontrolle)

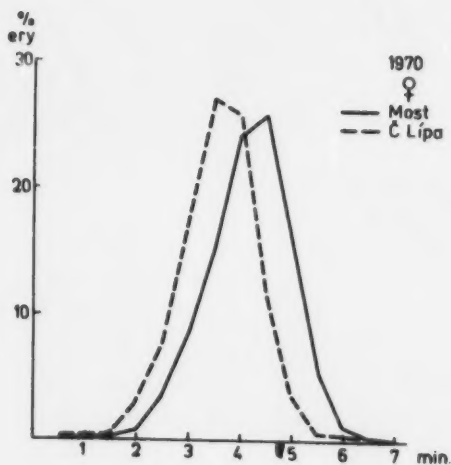


Abb. 6. Erythrogrammkurve der Mädchen; mittlere Zahl der pro Zeitintervall lysierten Erythrozyten (%) vom Jahre 1970 aus Most (expon.) und Ceska Lipa (Kontrolle); Rechtsverlagerung der Kurve = erhöhte Erythrozytenresistenz

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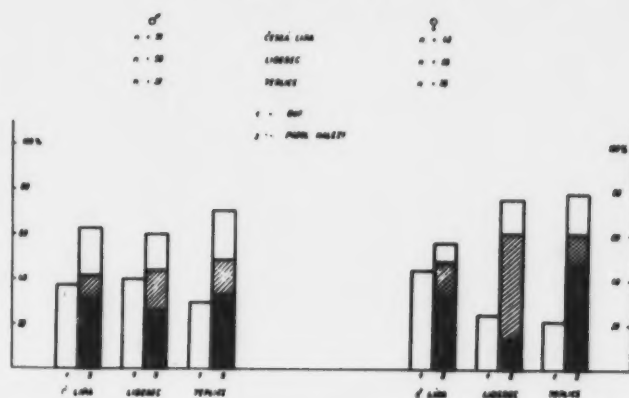


Abb. 7. Häufigkeit (%) des Befundes "normale Mundflora" (1) und von pathologischen Keimbefunden (2) in den Tonsillenkrypten; Herbst 1971, Teplice (expon.) sowie Ceska Lipa und Liberec (Kontrolle)

MURAMIDÁZA - 1972

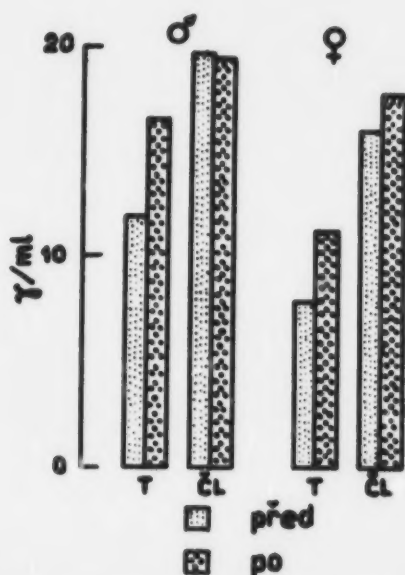


Abb. 8. Lysozymkonzentration im Speichel (mg/ml); Mittelwert: vor (pred) und nach (po) der klinischen Untersuchung des Jahres 1972 aus Teplice (expon.) und Ceska Lipa (Kontrolle)

Mädchen gleichsinnig; wir haben jedoch den Eindruck gewonnen, daß die Knaben auf eine Änderung der Immissionssituation schneller und stärker reagieren als die Mädchen.

In Nordböhmen bezog sich ein spezieller Teil der Untersuchung auf die Frage, ob sich die Kinder auch bzgl. der Keimbesiedlung der Tonsillenoberfläche und Tonsillenkrypten sowie hinsichtlich des Lysozymgehaltes des Speichels unterscheiden. Pfeifer (7) fand in Übereinstimmung mit dem klinischen Bild bei den Exponierten häufiger als bei den Nichtexponierten pathogene Keime (Abb. 7); Schmidt (8) sah bei den belasteten Kindern eine relative Erniedrigung des Muramidase spiegels, der als Parameter der unspezifischen Abwehrlage gilt (Abb. 8).

Unsere Studie hat darüberhinaus ergeben, daß sich die von tschechischen Autoren für tschechische Bevölkerungskollektive ausgearbeitete Methode der Gruppendiagnostik vernünftig und erfolgreich auch auf andere Populationen anwenden läßt. Unter der Voraussetzung, daß man die einzelnen Populationen mit Erfolg zumindest orientierend standardisiert hat, sind die mit dieser Methode gewonnenen Daten im Prinzip international vergleichbar.

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AIR POLLUTION: METHODS TO STUDY ITS
RELATIONSHIP TO RESPIRATORY DISEASE IN
BRITISH SCHOOLCHILDREN

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ABSTRACT

This paper describes the design and some of the methods used in a study of the relationship between air pollution and childhood respiratory disease.

The data were collected in the first year of a four year mixed longitudinal study intended to detect effects of changes in air pollution levels on respiratory disease in children.

Two aspects of methodology are discussed:- first the selection of survey questions concerning respiratory illness on the basis of the association of these reported illnesses with impaired peak expiratory flow rates; secondly, the use of quantal response regression to estimate the effects of atmospheric smoke and sulphur dioxide on respiratory disease after allowing for the effects of interfering factors (e.g. age, sex and social class).

Analysis by this method on a subsample of the study children showed a positive association between some of the selected reported illnesses and both smoke and sulphur dioxide.

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1. Introduction

There is substantial evidence that children in areas with high concentrations of atmospheric smoke and sulphur dioxide have more respiratory disease than those in areas of low pollution (1,2). The objective of our study is to determine whether changes in respiratory disease prevalence in children over successive years are related to changes in measured levels of air pollution. The opportunity to test this hypothesis has arisen in Britain since the introduction in 1956 of the Clean Air Act which prohibited the emission of dark smoke by industry. The domestic provisions of the Act gave Local Authorities power to set up Smoke Control Areas in which the burning of fuels other than 'smokeless fuels' was forbidden. Smoke Control Areas are still being designated and smoke emissions and concentrations are decreasing over time. (3).

This paper discusses some of the methodology of the study.

2. Method

2.1 Study Design

The study is being carried out in association with a national study of the health and growth of approximately 11,000 school-children aged 5 to 11 years. All children attending selected primary schools in 28 areas of England and Scotland are being examined annually. The areas represent a random sample stratified by an index designed to indicate their relative wealth. The sample was weighted to include a higher proportion of poorer areas.

TABLE I

Study Design

Age (years)	11	A	B	C	D
	10	B	C	D	E
	9	C	D	E	F
	8	D	E	F	G
	7	E	F	G	H
	6	F	G	H	I
	5	G	H	I	J

The design of the study is shown in Table I in which cohorts are identified by different letters. This mixed longitudinal design lends itself to several methods of analysis. For example, we can compare respiratory disease prevalence in equivalent age groups over successive years. We can also trace the changes in respiratory disease prevalence in any cohort and compare these with the changes experienced by another cohort which may have been exposed to different levels of pollution.

2.2 Measurement of Respiratory Disease

2.21 Questionnaires

Self-administered questionnaires are completed by parents of children in the study. Questions are asked about each child's

respiratory disease episodes and symptoms as shown in Table II and about each family's social and economic status.

TABLE II

List of questions about child's health

1. Does he or she usually cough first thing in the morning?
(Exclude clearing throat or single cough).
2. Does he or she usually cough during the day or at night?
(Exclude clearing throat or single cough).
3. Does his or her chest ever sound wheezy or whistling?
4. Do colds usually go to his or her chest?
5. Has he or she had earache in the last 12 months?
6. Has he or she suffered from any of these illnesses in the last 12 months?
 - Asthma
 - Bronchitis
 - Pneumonia
7. Has this child stayed in hospital overnight or longer in the last 12 months?
Please give the reason for each separate admission and the length of stay.
8. Which of the following words do you think best describes this child's health?
 - Excellent
 - Good
 - Fair
 - Poor
9. Has this child been seen by a doctor within the last two weeks?

2.22 Peak expiratory flow rates

Peak expiratory flow rates are measured using Wright Peak Flow Meters. Five readings are taken from each child and the mean of the last three is used in analysis. Height and weight are measured at the same time. All measurements are taken by trained nurses in each area in the presence of one of the fieldworkers

from our department who remeasures 12% of the children. The comparability of the measurements taken by the three fieldworkers is also assessed periodically. These data from the nurses and the fieldworkers are used to estimate the size of measurement error due to differences in machines and techniques.

2.3 Measurement of Air Pollution

Smoke and sulphur dioxide are sampled using a standardized hydrogen peroxide sampler as recommended by the Organisation for Economic and Cooperative Development. The same type of meter is used in the United Kingdom National Study of Air Pollution conducted by Warren Spring Laboratory.

A meter is sited at or within half a mile of each school in the study and 24 hour readings are obtained. Reflectometry on smoke stains and titration of sulphur dioxide are performed under the supervision of people trained by Warren Spring Laboratory.

3. Methods of Analysis

3.1 Choice of Respiratory Disease Measurement

The quality control system described above allowed us to compare the peak expiratory flow measurements obtained by one of our fieldworkers using a standard meter with those obtained by a nurse using a different meter on the same sample of children. Our analyses indicated that most of the measurement errors were due to differences between meters rather than between observers. The meter differences were present even after recent calibration. Table III shows the magnitude of the difference between peak expiratory flow rates obtained on one meter by one fieldworker and

TABLE III

Mean differences in peak expiratory flow rate (PEFR) between
five meters and a standard meter

Nurses' Meters	No. of Children	Mean Difference (l/min)	Standard Error	p (t-test)
A	81	17.0	2.0	< .001
B	97	14.9	1.9	< .001
C	56	30.4	4.1	< .001
D	32	-9.4	4.2	< .05
E	29	16.6	4.1	< .001

Each child's PEFR was measured on a nurse's meter and a standard meter. Five readings were taken with each meter. The meters were used in random order.

those obtained by nurses using some of the other meters. In this table each of the meters A to E have been used by more than one nurse. In addition to the differences shown, readings tended to vary over the time that a meter was in service. It seems likely that the differences in peak flow rates expected between areas of high and low pollution would be small in comparison with the magnitude of inter-meter variation shown in the table.

The biases arising from differences between meters can be eliminated in small surveys, by randomly allocating the meters over the whole study population. However, in studies where populations

are being measured in many widely separated areas it is not administratively feasible to do this.

One of the methods of overcoming this difficulty is to use reported illnesses which are associated with reduced peak flow rates. This method was tested on a sample of the children examined in 1973. For each question the population was divided into those replying yes and those replying no. The peak flow rates for these groups were adjusted for differences in age, sex, height, weight and which meter had been used (analysis of covariance) and then compared. The adjusted mean flow rates for the two groups for each question are given in Table IV. The difference between the rates and the probability of the difference arising by chance are also given.

The data suggest that the first six questions in the table may be used as indicators of lower respiratory tract disease.

3.2 Statistical Techniques for Handling Reported Respiratory Disease

A quantal response (i.e. yes or no, in this case) was available for each question. We wanted to know first whether age, sex and social class were associated with the response, second whether, after adjustment for these variables, smoke and SO_2 were also related to the response and, third, how the proportion of people giving a positive response changed with change in smoke and SO_2 .

Simple tabulation of the data showed that age, sex, social class and area (or pollution level) were each separately associated with positive responses. A model was required to predict the response using age, sex, social class, smoke and SO_2 as predictors. The commonly used multiple regression analysis requires that the predicted variable is continuously and normally distributed at each

TABLE IV

Peak expiratory flow rates, (PEFR), adjusted for
age, height, weight and meter, by reported disease

<u>Question</u>	<u>% reporting symptom (Total-3115)</u>	<u>PEFR(1/min) if no symp- tom</u>	<u>PEFR (1/min) if has symp- tom</u>	<u>Difference in PEFR (1/min)</u>	<u>Probability of differ- ence arising by chance</u>
1. Asthma in last year	1.8	242.2	212.8	29.4	< 0.0005
2. Wheeze	10.2	243.2	226.2	17.0	< 0.0005
3. Fair/ Poor Health	5.4	242.3	227.0	15.3	< 0.0005
4. Bron- chitis in last year	5.3	242.5	228.0	14.4	< 0.0005
5. Cough	8.4	242.6	231.2	11.5	< 0.0005
6. Colds to chest	25.5	244.0	233.7	10.2	< 0.0005
7. Doctor visit in last 2 weeks	9.4	242.1	237.7	4.4	< 0.10
8. Ear- ache in last 12 months	27.8	242.0	241.1	0.9	< 0.25
9. Hospi- tal for upper respira- tory dis- ease in last 12 months	2.0	241.6	240.8	0.8	< 0.90

value of the independent variables if the statistical tests are to be valid. Since the response was not continuously distributed, a regression method specially designed to handle quantal data was used.⁽⁴⁾ This provides a regression equation which predicts the probability that a group of individuals with characteristics described by the independent variables would give a positive response to any particular question. Each regression coefficient could be tested for statistical significance and the significance of combinations of variables can be calculated.

This method has been used on some of the information collected during 1973. An equation was computed for the 1,816 children for whom sex, age, social class and ambient air pollution levels were known. The air pollution levels used were the mean smoke and SO_2 for November 1973. These variables were used to predict the logit^{N} of the proportion of subjects reporting colds to the chest. None of the independent variables were correlated with any other, except smoke with SO_2 . These two showed such high correlation that they were entered into separate equations. Both pollutants were found to be significantly associated with a history of colds going to the chest ($p < .05$). The equation for predicting colds to the chest showed increased risk for this reported illness for males, younger children, those in lower social classes and those living in areas with high smoke or SO_2 pollution.

By appropriate substitution in the equation, the proportion of children who would be expected to have colds to the chest was

^N The logit used in the analysis was $0.5 (\ln (P/1-p))$ where P is the proportion of children with a characteristic.

estimated for the group at greatest risk (males, aged 5, social class V).

Over the range of smoke levels in this analysis ($10\text{--}130\text{ }\mu\text{g}/\text{m}^3$), it was predicted by the equation that for each increment of $10\text{ }\mu\text{g}/\text{m}^3$ of smoke (ignoring SO_2), 0.77% more of this population would have colds to the chest. In the group at least risk (females, aged 11 in social class I) approximately 0.40% of the population would be affected with each $10\text{ }\mu\text{g}/\text{m}^3$ increment in smoke. Similar results were obtained for SO_2 , ignoring smoke.

Using the same technique, no significant relationship was found between air pollution (smoke and SO_2 separately or combined) and the other respiratory diseases listed in Table IV. The relationships however were always in the direction of more disease in more polluted areas.

Both smoke and SO_2 were significantly associated with respiratory disease defined as a positive answer to at least one of the six questions indicative of lower respiratory tract disease ($p < .005$). This relationship is still under study.

4. Comment

Reported illness provides a useful measure of respiratory disease in children. Questions can be selected on the basis of their relationship to impaired peak expiratory flow rates. Binary data of this type can then be analysed using a quantal response regression which predicts the probability of any defined group having a reported illness.

The model we have used assumes a linear relationship between a set of predicting or independent variables and the logit of the

proportion of subjects reporting illness. This model appeared to fit the data well ($P=0.5$, χ^2 for fit).

We have used the predictive quality of the equation to estimate the changes to be expected in the prevalence of colds to the chest in the groups at highest and lowest risk (as judged by the equation). These predictions suggest that diminution of smoke or SO_2 levels from $130 \mu\text{g}/\text{m}^3$ to $10 \mu\text{g}/\text{m}^3$ would result in a decline in prevalence from 49% to 40% in the highest risk group and from 17% to 12% in the lowest risk group.

These predictions have been made for the extreme groups and may carry rather large standard errors. A method for calculating the standard error is not yet available however, so we may only suggest the change in the prevalence of 'colds to the chest' over the given range of pollution levels lies somewhere between 5% and 9%.

Quantal regression has thus permitted us to make predictions from prevalence data about the changes we might expect to find in longitudinal data. We must now await the end of the study to see whether the changes occurring in respiratory disease prevalence as air pollution levels change correspond to our predictions.

5. Acknowledgements

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EPIDEMIOLOGIC STUDIES OF ADVERSE HEALTH EFFECTS ASSOCIATED WITH EXPOSURE TO AIR POLLUTION

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ABSTRACT

Epidemiologic studies of the effects of air pollution have been conducted by the Human Studies Laboratory of the U.S. Environmental Protection Agency since 1969. These studies have been carried out in groups of communities selected to be similar with respect to climate and demographic characteristics but to differ with respect to air pollution levels. Measurements of health status within each community were made in a manner which permitted differences to be associated with differences in exposure to pollution. Particular effort was made to select the groups of communities to provide gradients for particular pollutants or combinations of pollutants in the hope that the total data obtained might provide evidence concerning the relative significance of specific pollutants, especially sulfur dioxide (SO_2) and the total suspended particulates (TSP).

The results of these studies have shown consistent associations of impaired health status with exposure to higher levels of pollution. They have, however, left a number of problems unanswered including the one concerning the relative significance of SO_2 or TSP. On the other hand the studies indicated that the atmospheric levels of suspended sulfates may be more directly related to impaired health than is either SO_2 or TSP.

As the results of chronic exposure, studies were analyzed and the data interpreted, ranges of current or prior exposure values were developed to represent the "worst case" and the "least case" air pollution level which might have been incriminated in a causal manner with the adverse health effects measured (Table 1). Then within these ranges "best judgement" estimates were made concerning the levels that in the opinion of the investigators most probably were related to the increased adverse effects.

For the short-term studies comparisons of the variation in health status were made with 24 hour daily mean levels of pollution (Table 2).

The studies of chronic respiratory disease¹⁻⁴ indicated that the relative contribution of air pollution alone ranged from one-third to one-seventh that of cigarette smoking as a determinant of chronic bronchitis prevalence in communities. The sum of the evidence suggested that, while personal cigarette smoking was the largest determinant of bronchitis prevalence among parents of school children, air pollution itself was a significant and consistent contributing factor, leading to increased bronchitis rates in nonsmokers as well as in smokers from polluted communities.

Attempts to assess the length of residence in polluted areas required for development of excess bronchitis rates suggested that immigrants into polluted areas reported excess chronic bronchitis after two to seven years of exposure.

TABLE 1
SUMMARY OF CHESS STUDIES RELATING LONG-TERM POLLUTANT EXPOSURES INVOLVING SULFUR DIOXIDE, TOTAL
SUSPENDED PARTICULATES AND SUSPENDED SULFATES TO ADVERSE EFFECTS ON HUMAN HEALTH

Adverse Effect on Human Health	Type of Estimate	Duration of Exposure (Years)	Annual Average Levels Linked to Adverse Health Effects ($\mu\text{g}/\text{m}^3$)		
			Sulfur Dioxide	Total Suspended Particulates	Suspended Sulfates
Increase in Prevalence of Chronic Bronchitis in Adults	Worst Case	3	62	65	12
	Least Case	10	374	179	20
	Best Judgment	6	95	100	15
Increases in Acute Lower Respiratory Tract Infections in Children	Worst Case	3	92	65	7.2
	Least Case	3	177	102	15
	Best Judgment	3	95	102	15
Increase in Frequency or Severity of Acute Respiratory Illness in Otherwise Healthy Families	Worst Case	1	50	104	14
	Least Case	3	210	159	16
	Best Judgment	3	106	151	15
Subtle Decreases in Childhood Ventilatory Function	Worst Case	1	57	96	9
	Least Case	9	435	200	28
	Best Judgment	8-9	200	100	13

TABLE 2
SHORT-TERM EXPOSURES:
POLLUTANT THRESHOLDS FOR ADVERSE EFFECTS
(BEST JUDGMENT)

EFFECT	THRESHOLD, 24-hour $\mu\text{g}/\text{m}^3$		
	SO ₂	TSP	SS
AGGRAVATION OF SYMPTOMS IN ELDERLY	>365	80-100	8-10
AGGRAVATION OF ASTHMA	180-250	70	8-10

In the best judgement of the investigators, excess chronic bronchitis in the Salt Lake Basin of Utah could reasonably be attributed to annual mean sulfur dioxide levels of 92 to 95 $\mu\text{g}/\text{m}^3$ and/or suspended sulfate levels of 15 $\mu\text{g}/\text{m}^3$. In the other areas, the investigators judged that the lowest annual mean pollutant concentrations which could reasonably be associated with excess chronic bronchitis were past exposures to 100-177 $\mu\text{g}/\text{m}^3$ sulfur dioxide, 80-118 $\mu\text{g}/\text{m}^3$ total suspended particulates and 9-14 $\mu\text{g}/\text{m}^3$ suspended sulfates.

From these data, it appeared that excess bronchitis may be associated with community exposures to sulfur oxides alone, in the form of annual levels of 92 to 95 $\mu\text{g}/\text{m}^3$ SO_2 and 15 $\mu\text{g}/\text{m}^3$ suspended particulate sulfates. When higher levels of particulate matter were present, annual exposures to 100 $\mu\text{g}/\text{m}^3$ SO_2 , 120 $\mu\text{g}/\text{m}^3$ total suspended particulate and 14 $\mu\text{g}/\text{m}^3$ suspended sulfate were associated with excess bronchitis.

Lower respiratory disease (LRD) studies of children⁵⁻⁶ indicated that for single and repeated episodes of croup and repeated episodes of any LRD, families of children who had lived for three or more years in the high exposure communities reported more illness across all ages of children from 0 to 12 years than did their counterparts in the less polluted communities.

It is interesting that larger increases in total LRD were observed in the high pollution community of the Salt Lake Basin

study than in the high pollution communities in another Rocky Mountain study area. Also, the mean annual suspended sulfate concentration was higher in the high pollution community in the Salt Lake Basin study than in the other Rocky Mountain study but the opposite was true for SO_2 . This suggested that the increases in LRD frequency were more likely associated with suspended sulfates than with SO_2 .

In the best judgement of the investigators, it seemed reasonable to conclude that there is a positive association between lower respiratory disease frequency in children and pollution exposure, and that excess respiratory disease may be associated with community exposures to approximately $95 \mu\text{g}/\text{m}^3$ SO_2 and $15 \mu\text{g}/\text{m}^3$ suspended sulfates.

Acute respiratory disease studies of families in Chicago⁷ and New York studies⁸ showed that, with the exception of fathers, a consistent excess acute respiratory disease rate was reported among family members living in more polluted neighborhoods. The relative excess varied from 3 to 40 percent. A conservative estimate would be that exposures to $210 \mu\text{g}/\text{m}^3$ SO_2 with $104 \mu\text{g}/\text{m}^3$ total suspended particulates and approximately $16 \mu\text{g}/\text{m}^3$ suspended sulfates was associated with a 5 to 20 percent excess of acute respiratory illness in various family members.

The Chicago study¹ also provided evidence of increased susceptibility to epidemic A₂/Hong Kong influenza among otherwise healthy families exposed during the previous three years to atmospheric levels of 106 to 119 $\mu\text{g}/\text{m}^3$ SO₂, 151 to 159 $\mu\text{g}/\text{m}^3$ total suspended particulates, and 14 $\mu\text{g}/\text{m}^3$ suspended sulfates.

Pulmonary function studies⁹⁻¹⁰ showed that ventilatory function of elementary school children, measured by the three-quarter second forced expiratory volume (FEV_{0.75}), was diminished in areas of elevated exposure to sulfur oxides. In New York only the older children (age nine to 13 years) who had been exposed to substantially elevated pollutant concentrations for the first five to ten years of life suffered reduced ventilatory function. The best available estimates of these remote annual average exposures were as follows: sulfur dioxide, 131-435 $\mu\text{g}/\text{m}^3$, total suspended particulates, 75-200 $\mu\text{g}/\text{m}^3$, suspended sulfates, 18-28 $\mu\text{g}/\text{m}^3$.

Ventilatory function in white children exposed to suspended sulfate concentrations of about 9.5 $\mu\text{g}/\text{m}^3$ was lower than that of white children exposed to concentrations of about 8.3 $\mu\text{g}/\text{m}^3$. Black children studied were all exposed to suspended sulfate concentrations of about 8.9 $\mu\text{g}/\text{m}^3$, and these children demonstrated no differences in ventilatory function.

From a Cincinnati study, it was conceivable that one year's exposure to $9 \mu\text{g}/\text{m}^3$ of suspended sulfates, in the presence of moderate levels of sulfur dioxide and total suspended particulates ($57 \mu\text{g}/\text{m}^3$ and $96 \mu\text{g}/\text{m}^3$, respectively) might alone account for reduced ventilatory function.

Among asthmatics and study subjects with cardiopulmonary illness in the Salt Lake Basin¹¹ daily attack rates were more consistently correlated with lower outdoor temperature than with any measured pollutant. Asthma attack rates were most closely related to stepwise increases in the levels of suspended sulfates. Virtually no relationship between SO_2 and attack rates appeared. Total suspended particulates and suspended sulfates were positively and stepwise correlated with daily asthma attack rates.

In New York, asthma attack rates were more consistently associated with daily suspended sulfate levels than with either SO_2 or TSP¹². The pattern of daily aggravation of symptoms in cardiopulmonary subjects in New York⁴ was very similar to that of asthma. Low temperatures were directly related to increased symptom rates in subjects with combined heart and lung disease. Elevated suspended sulfates were the only pollutant consistently associated with symptom aggravation.

It was the best judgement of the investigators that significant aggravation of cardiopulmonary symptoms could be

attributed to 24-hour suspended sulfate levels as low as 8-10 $\mu\text{g}/\text{m}^3$ on cooler days (20-40°F) or warmer days (41+°F). The investigators intuitively felt that the chemical composition and particle size involved in sulfate exposures were critical determinants of the threshold for the adverse response.

With regard to short-term exposures then it was evident that adverse health effects were attributable to suspended sulfate levels rather than to the observed concentrations of SO_2 and for TSP.

The identification of atmospheric suspended sulfates as an environmental pollutant of concern to health, it is now necessary to obtain sufficient information to recommend the extent to which emissions should be controlled to protect against them. Little is known about the formation of atmospheric suspended sulfates and even less is known about the means to control them. To develop adequate information about this need it is also necessary to determine if all sulfates are equally reactive; if sulfates are reactive because of the chemical properties associated with specific chemical compounds; or because of physical properties such as particle size or pH; and if sulfates are equally reactive in humid and dry air and at high and low temperatures. These biological issues must be addressed and satisfactorily resolved, because our strategies to protect human health may be critically dependent on the nature of the

sulfate-biologic response relationship. Until more definition of these issues is achieved, however, our findings indicate strongly that we are just beginning to learn about the real impact of atmospheric pollution on human health.

These issues are being addressed in the current research program of the Human Studies Laboratory.

SUMMARY

Epidemiologic studies of the health effects of air pollution in the United States have indicated that both acute and chronic health effects are associated with exposure to ambient air containing approximately $100 \mu\text{g}/\text{m}^3$ SO_2 , $100 \mu\text{g}$ TSP and $15 \mu\text{g}/\text{m}^3$ suspended sulfates. The levels of suspended sulfates were associated more closely and more consistently than were the levels of either TSP or SO_2 .

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PREDICTIVE MODELS FOR ESTIMATING THE HEALTH IMPACT OF FUTURE ENERGY SOURCES

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ABSTRACT

Decisions regarding future energy usage will depend on a number of major parameters, including those most essential to life, and must be based on consideration of the pollutants produced by the source, control methods for the pollutants, and, most important, the health effects produced by the energy source used.

Models for quantitating health effects on varying populations and the predictive capacity for assessing these effects have been developed and will be discussed; and, the types of studies that are needed to increase the required data base for this predictive capacity will be explored.

Results of a study examining visits to the emergency rooms in eighteen major hospitals in the City of Chicago during twenty-four hours on the same day of the week that was carried out for a period of eighteen months will be presented. Documentation of all admissions to the emergency rooms for cardiac, respiratory, and other diseases was maintained and levels of various air pollutants at the hospital and in the area of the residence from which the patients came to the hospital were evaluated. The study examines these relationships and their effect on the cardio-pulmonary system and how these results can be used in the predictive

model being developed. The model is based on the concept of a continual dose-response relationship between air pollutants and health and requires definition of various categories in the population at high risk. By quantitative definition of differences in disease at low and high pollution levels in those at high risk and determination of the total numbers of these individuals in the population, the numbers that are affected at varying levels of pollution can be ascertained.

The extraordinary increase in the use of fuels for the production of energy for industrial use, transportation, and the production of electricity, has created serious problems of environmental contamination. The dilemma faced by all industrial societies is one of achieving and maintaining a healthy environment in the face of this apparent huge energy need and limited or inaccessible clean energy sources.

Some pollution accompanies any energy production and use. Decisions regarding future uses of alternative energy sources must, therefore, be considered with great care. While these decisions must examine many social, economic, and political factors, an essential parameter is the health effects; and, not only current, but future impact must be estimated for each energy source with increasing use, as well as for new and untried sources.

Pollutants frequently occur together, thus decisions regarding alternatives must consider two preliminary sets of questions in order to determine priorities for development of technology for the selective removal of individual pollutants. These questions are:

- 1) Which pollutants are the major health stressors?
- 2) What is the extent of the contribution, qualitatively and quantitatively, of each to etiology or pathogenesis of various diseases?
- 3) What meteorologic and other environmental factors contribute as environmental stressors?

A study examining this series of questions was recently carried out in the City of Chicago and will be discussed.

Critical questions which then must be asked concerning the health cost of a particular energy source include:

- 1) How many people are being adversely affected by pollutants from various energy sources, such as coal, oil, natural gas, and nuclear energy?
- 2) Who are the affected people and what diseases are caused or exacerbated by these substances?
- 3) How many more would be affected by the increased pollutants produced from a particular source for a given increase in energy production?

A model developed to begin to answer these critical questions in order to predict the impact on populations of changes in pollution levels engendered by qualitative or quantitative changes in fuel sources for

FIGURE 1

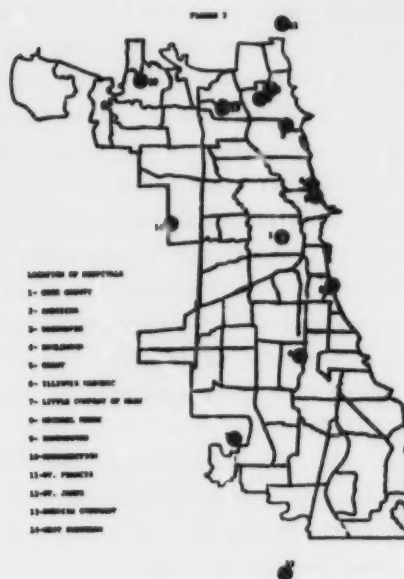
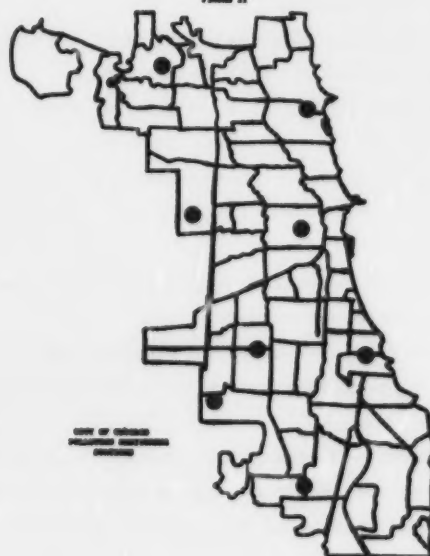


FIGURE 2



for energy use, will be presented.

HOSPITAL EMERGENCY ROOM STUDY

METHODS:

Emergency room admissions for all major respiratory and cardiac causes were monitored from midnight on the Monday of each week to midnight on Tuesday for eighteen months in fourteen hospitals scattered throughout the City of Chicago. (Figure I) A form listing each major cardiac and respiratory disease was used by the nurse in charge of the emergency room to enter a diagnosis for each individual seeking care. In addition, the age, sex, race, and place of residence were noted. These data were collected each week and computerized.

Pollution and Meteorologic Measurements:

The City of Chicago maintains a continuous monitoring network of eight stations which measure SO_2 , coefficient of haze (COH), CO, and for a lesser period of time, NO_x . (Figure II) In addition, a twenty station network measured twenty-four hour levels of SO_2 and particulate, three days each week. Using these data and with the knowledge of the residence location of each individual who was admitted to the emergency rooms, two indices of air pollution exposure were used in analyzing the data. The first was a citywide average, or arithmetic average of air pollution levels observed at all functioning monitoring stations. The second was a weighted average of levels at these stations where, for a given hospital, if n_i = the number of subjects admitted for cardiac or respiratory causes who reside in areas closest to monitoring station i for the entire period of study.

$N = \sum_i n_i$ = the total number of subjects examined for cardiac or respiratory causes,

P_{id} = The air pollution level observed at monitoring station i for a given day, d ,

The weighted pollution average, W_d , on a day d is defined by the formula:

$$W_d = \sum_i \frac{n_i}{N} \cdot P_{id}$$

In justifying the use of the weighted average as a valid indication

of air pollution exposure, two assumptions were made:

- 1) Air pollution levels observed at a given station should generally reflect the exposure in areas closest to that station, and
- 2) The population from which a given hospital drew its patients was reasonably stable, at least for the duration of the present study, so that the observed proportion ($\frac{n_i}{N}$) of patients residing in the neighborhood of Station i would be a reasonable estimate of the actual proportion of the number of individuals residing near Station i most likely to seek treatment at that hospital.

A consideration of the formula for the weighted average shows that this quantity will tend to reflect exposure in areas where there is a high proportion of individuals seeking treatment, whereas, the citywide average gives all areas equal weight. Since the distribution of place of residence of individuals who seek emergency treatment at a particular hospital is far from uniform (Figure III) but instead, reflects socioeconomic factors and accessibility to the hospital, the use of a weighted average appears justifiable.

Each hospital then compared admissions to its emergency week from week to week, throughout the eighteen months of study in relation to variations in these pollution levels.

As a preliminary step in determining whether significant associations held between the number of emergency room admissions and air pollution, multiple linear regression techniques were applied to the data. To briefly summarize this method, a linear relationship is assumed to hold between a so-called "dependent" variable (the number of admissions, in this case) and a set of "independent variables, or predictors, whose behavior may influence the behavior of the dependent variable. Because of measurement error in the dependent variable, observed values of the dependent variable will tend to fluctuate about the hypothetical line or plane defined by the linear relationship. Multiple regression analysis provides estimates of the values of the dependent variable in terms of the independent variables, such that the deviation of the observed values of the dependent variable from the estimated values is minimized. The percentage of total variation in the dependent variable explained by the independent variables (R^2) can also be calculated and tested for statistical significance. When variables are observed in time, as in this case, rather than under controlled laboratory conditions, it is possible that an

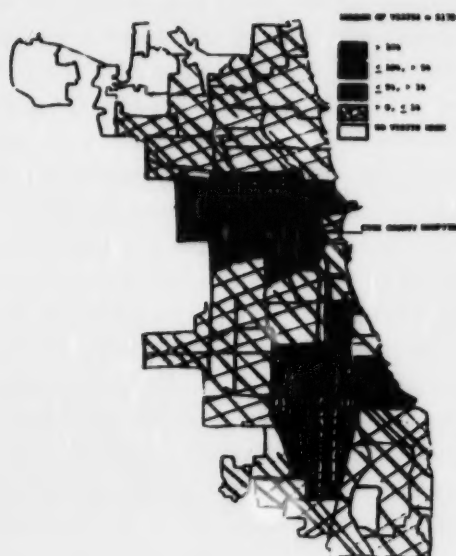


Figure III : Distribution by place of residence of patients making cardiac/respiratory emergency room visits to Cook County Hospital (Chicago)

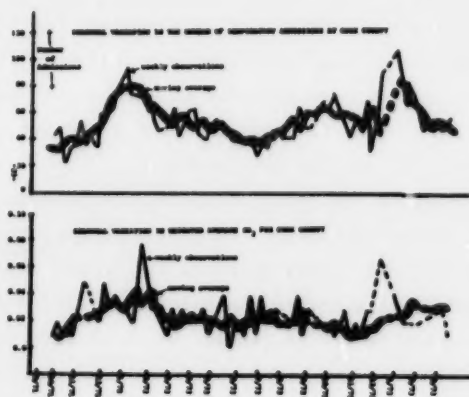


Figure IV : Chicago cardiac/respiratory emergency room admission study. Seasonal variation in SO_2 and respiratory admissions from October, 1971 through March, 1973. Cook County.

apparent association between them may be due to the action of unobserved variables correlated with some of the observed variables. Most of the variables in the present study are correlated in time; for example, Figure IV shows pronounced seasonal variation in the number of respiratory admissions and in the weighted SO_2 average. Since many variables exhibit a similar relationship in time, but are clearly not factors which precipitate episodes of chest illness, all variables in the present study were seasonally adjusted before applying any statistical technique to the analysis of the data. Each variable was seasonally adjusted by subtracting from its observed value on a given day, a "moving" average of the four values, one and two weeks before and following the day in question. The moving average serves as a rough estimate of seasonal trend with the irregular or short-term component of variation removed; hence, the deviations of the values for individual days from the moving average should be independent of season of year and reflect short-term variability only. As an example, the heavy black curves in Figure IV represent the moving average about which individual daily values fluctuate, and in Figure V, it can be seen that the seasonally adjusted values plotted against time, no longer exhibit seasonal variation.

The number of emergency room admissions on a given day can be affected by conditions which actually have no bearing on actual illness; e.g., some individuals tend to stay at home, even when requiring immediate medical attention, because of inclement weather. Since air pollution is inversely associated with factors such as heavy precipitation, which tends to disperse air pollution particles, a direct association of admissions with air pollution may be observed, merely because individuals stayed at home during heavy precipitation which resulted in low air pollution levels. Various types of climatological conditions were therefore added to the model in order that their effects could be separated from the effects of the air pollutants.

The addition of the climatological variables to the model resulted in a total of twelve independent variables as compared to thirty days of observations for Cook County Hospital in winter. Mathematically, the addition of more variables to the model will always result in a larger value of R^2 , which is the percentage of total variation in the dependent variable explained by the model; however, when the number of variables is large compared to the number of observations, the estimate of the

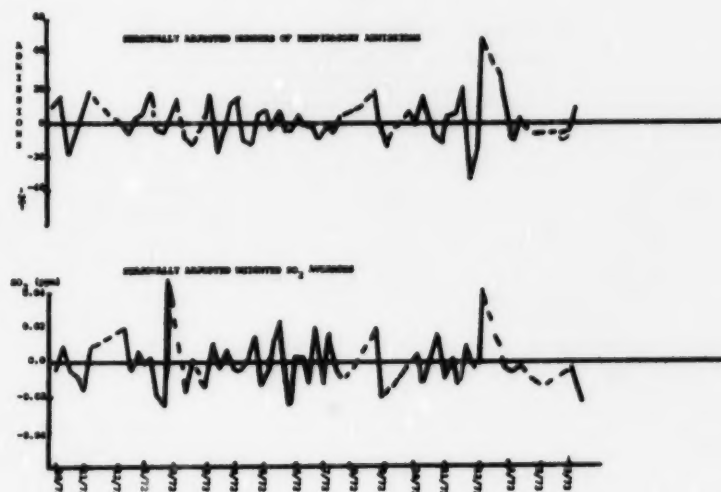


Figure V : Chicago cardiac/respiratory emergency room admissions study. Seasonally adjusted respiratory admissions and SO₂ levels from October, 1971 through March 1972 for Cook County Hospital

Figure VI

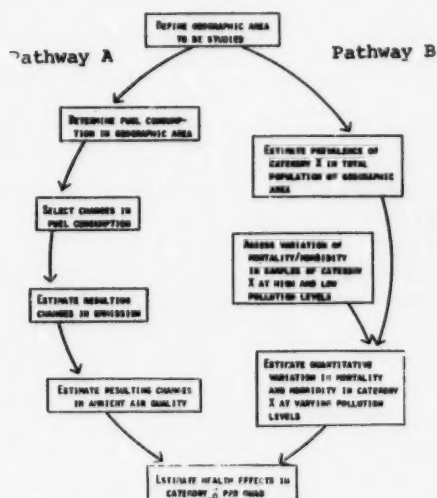


Figure VI : Model for Quantitating and Predicting Health Impact of Energy Consumption

TABLE I

Chicago Cardiac/Respiratory Emergency Room Admissions Study

Distribution of Number of Em. Room Visits by Diagnosis

Hospital is Cook County

Number of Tuesdays in Study is 80

(9/14/71-3/27/72, no information for 2/29/72)

Diagnosis	Per Cent of Total	Number	Average per Tuesday
Asthma	17.1	884	11.1
Acute Bronchitis	38.1	1974	24.7
Pneumonia	7.1	360	4.6
Sinusitis	3.5	182	2.3
Acute Tracheobronchitis	0.0	2	0.0
Acute Respiratory	3.1	163	2.0
Other Respiratory	22.0	1141	14.3
Myocardial Infarction	0.7	35	0.4
Congestive Heart Failure	1.2	62	0.8
Other Cardiac	7.1	360	4.6
Total Respiratory	91.0	4713	58.9
Total Cardiac	9.0	465	5.8
Total Cardiac/Respiratory	100.0	5178	64.7

TABLE II

Chicago Cardiac/Respiratory Emergency Room Admissions Study

Distribution of Number of Emergency Room Visits by Diagnosis
13 Hospitals (excluding Cook County)

Diagnosis	Per Cent of Total*	Number	Average per Tuesday*
Asthma	11.3	773	10.3
Acute Bronchitis	41.4	3480	32.6
Pneumonia	8.6	564	7.3
Sinusitis	0.4	25	0.3
Acute Tracheobronchitis	2.0	104	1.4
Acute Respiratory	0.3	18	0.1
Other Respiratory	5.4	349	4.6
Myocardial Infarction	15.6	832	10.7
Congestive Heart Failure	8.7	536	7.0
Other Cardiac	6.3	384	5.0
Total Respiratory	69.4	4317	56.7
Total Cardiac	30.6	1742	22.6
Total Cardiac/Respiratory	100.0	6059	79.3

* The number of observations varies from one hospital to another. Therefore, the percent of total above is the average percentage over all the individual hospitals and the average per Tuesday is the sum of the Tuesday averages over the individual hospitals.

variation of the observations about the estimated regression line or plane (residual mean square) can increase, particularly if the additional variables do not account for a large portion of the variation. To find the "best" predictive model among the twelve independent variables necessitates making 3^{12} , or 4,096, separate regression analyses for each choice of the dependent variable. Therefore, a stepwise regression procedure was applied, which ordinarily provides a good, if not optimal, solution. Briefly, on the first step of this procedure, the independent variable having the highest correlation with the dependent variable is selected first, and on successive steps, other independent variables are selected which have the highest correlation with the independent variable when the effects of the variables selected on preceding steps are eliminated. The procedure continues in this fashion until either all variables are selected, or until the contribution of additional factors is negligible, according to some criterion.

RESULTS:

The hospitals selected were generally the larger facilities scattered throughout the city. Admissions to the emergency room for most of them were relatively small for each diagnostic category day and frequently reflected the inaccessibility of the private physician because of the time of occurrence of illness. Cook County Hospital, the largest hospital in the city, received almost 50% of all admissions, reflecting its use as a primary care facility by the lower socioeconomic population, mostly inner city blacks, who generally had no physician or ongoing medical care. Table I reveals the frequency distribution of admissions by diagnostic categories, Table II, those of all the other hospitals, except Cook County. While the pattern generally is similar, myocardial infarction appears to be more frequent in the other hospitals. This is because at Cook County these patients are admitted directly to the hospital and do not go through the emergency room.

The analyses carried out to date for hospitals other than Cook County reveal some evidence of associations between some pollutants and some diseases, particularly hospitals like Englewood, which also services a majority of black patients. The results, however, are not consistent and, while this may reflect the manner in which the emergency rooms are used, no conclusions can be drawn. Further, analyses are being carried out, and

TABLE III
Chicago Cardiac/Respiratory Admission Emergency Room Study. Stepwise Regression Model Found by Stepwise Procedure Explaining Variation in the Numbers of Admission for Selected Conditions. All Variables are Seasonally Adjusted. ** Hospital is Cook County. Sources: 10 Winter, 6-73.

Condition	Coeff., std. error, r^2 to test coeff., del. from model for independent variables											No. of cases	r^2	F
	WIND ¹	WIND ²	WIND ³	Temp	Water precip	Humid ⁴	WIND ⁵	WIND ⁶	Wind speed	Rel. humid.	Sunshine			
Asthma	0.64 ^{**} 0.30 [*] 1.30 [*]				-4.37 [*] 1.47 [*] 7.73				-0.39 [*] 0.39 [*] 3.67		-0.05 [*] 0.43 [*] 7.59 [*]	0.19	4	0.44 5.33 [*]
Acute Bronchitis	2.96 [*] 1.31 [*] 3.07 [*]				-0.38 [*] 0.39 [*] 3.73				-0.39 [*] 0.39 [*] 3.73		0.73 [*] 0.64 [*] 1.30	-1.43	4	0.39 3.47
Pneumonia	1.03 [*] 0.37 [*] 1.79 [*]				-1.61 [*] 1.09 [*] 3.30	0.39 [*] 1.00 [*] 0.59			-0.34 [*] 0.40 [*] 1.40		0.33 [*] 0.40 [*] 2.60	0.50	5	0.43 3.97 [*]
Myocardial Infarct									0.67 [*] 0.63 [*] 1.17			0.14	1	0.04 1.17
Cong. Heart Fail				0.33 [*] 0.01 [*] 4.55 [*]	-0.04 [*] 0.03 [*] 4.55 [*]	0.51 [*] 0.30 [*] 3.61		-0.44 [*] 0.36 [*] 3.30		0.41 [*] 0.41 [*] 3.49	0.40 [*] 0.40 [*] 7.03 [*]	0.17	4	0.54 4.54 [*]
Total Resp.	4.74 [*] 1.49 [*] 3.91 [*]			-0.43 [*] 0.31 [*] 3.90			-14.10 [*] 4.57 [*] 9.63 [*]					-3.79	3	0.40 3.97 [*]
Total Cardiac					2.43 [*] 1.96 [*] 3.92					0.39 [*] 0.40 [*] 3.95		0.01	1	0.30 3.09 [*]

* Model with smallest residual mean square.

** Example: BROWNS and CROWN.

1 "WIND" means "weighted average," e.g., "WIND¹" = weighted W₁ average.

2 BROWNS is an index of whether the wind blows from the north or west; positive values indicate easterly winds, negative values indicate westerly winds.

3 CROWN is an index of whether the wind blows from the north or south; positive values indicate northerly winds, negative values indicate southerly winds.

and this analysis will be limited to Cook County Hospital for the winter months (November, 71 - April, 72 and November, 72 - March, 73).

The best models found by the stepwise procedure (smallest residual mean square) for various choices of the dependent variable are presented in Table III and summarized in Table IV. They reveal that emergency entry for respiratory causes, particularly total respiratory, acute bron-

TABLE IV
Chicago Cardiac/Respiratory Admission Emergency Room Study. Summary of Table III Showing Stepwise Regression Results. Signs of Regression Coefficients and Statistical Significance of Coefficients Indicated. Hospital is Cook County. Winter.

Condition	WIND ¹	WIND ²	WIND ³	Temp	Water precip	Humid ⁴	WIND ⁵	WIND ⁶	Wind speed	Rel. humid.	Sunshine	Day cover (cloudless)	No. of cases	r^2
Total Resp.	(+)			(-)			(-)	(From W)					3	.40 [*]
Asthma	(+)				(-)				(-)		(-)		4	.44 [*]
Acute Bronchitis	(+)			(-)			(-)	(From W)				(+)	4	.39
Pneumonia	(+)					(-)	(+)	(From S)		(-)		(+)	5	.43 [*]
Total Cardiac		(+)			(+)					(+)			3	.30 [*]
Myocardial Infarct								(+)	(From S)				1	.04
Cong. Heart Fail			(+)	(-)	(-)		(+)	(From S)	(-)	(-)			4	.54 [*]

(-) = Negatively correlated

(+) = Positively correlated

* = Statistically significant at 5% level

1 "WIND" means "weighted average," e.g., "WIND¹" = weighted W₁ average

2 BROWNS is an index of whether the wind blows from the north or west; positive values indicate easterly winds, negative values indicate westerly winds.

3 CROWN is an index of whether the wind blows from the north or south; positive values indicate northerly winds, negative values indicate southerly winds.

chitis and pneumonia, appear to be strongly associated with increases in SO_2 , but not with CO . On the other hand, congestive heart failure correlates positively with carbon monoxide and negatively with temperature. Other factors which appear to add significantly to the same relationships include absence of sunshine and reduced windspeed for asthma, and reduced windspeed for congestive heart failure.

The trend of these analyses, in addition to those achieving 5% levels of significance, is generally in the appropriate direction. This study suggests that in this population of low socioeconomic blacks, using an emergency room as primary care physician, there appears to be a relationship between certain air pollutants, particularly SO_2 , and respiratory disease, and to a lesser degree between the incidence of congestive heart failure and CO levels.

These are very preliminary conclusions and additional analyses of the large amount of data gathered are being carried out.

PREDICTIVE QUANTITATION OF HEALTH EFFECTS OF AIR POLLUTANTS:

The emergency room study sought to further examine relationships of various categories of diseases of the respiratory and cardiac systems to different pollutants. Air pollution effects on chronic bronchitics, a disease known to be affected by irritant gases, have been studied by this and other groups in the United States and other countries. Additionally, we have examined the relationship between cardiac and respiratory deaths during an air pollution episode in the city. Many of these studies found increased morbidity and mortality at increasing levels of some of these pollutants, particularly SO_2 and particulate.

The model is proposed as a method, however, crude, to begin to answer the critical questions posed initially. It is based on a fundamental assumption (i.e. that there is no population threshold). The environment is essentially hostile and humans, as biological organisms, with varying degrees of resistance and adaptive capacities, are in continuous struggle with it. Any factor in the environment which increases environmental hostility or anything lowering the resistance of humans, decreases adaptability. Marginal people, that is those with poor adaptive capacity (i.e. because of serious lung disease, heart disease, asthma, or other advanced chronic diseases), were the populations examined in most studies of the effects of air pollutants on humans, since it was postulated that the

effects of irritant gases would be strongest on those with inadequate cardiac or pulmonary reserves.

A number of studies,^{1,2,3} including the Chicago Registry Study of Bronchitics⁴ suggest that there are increased illness and death rates in some members of the population at relatively low levels of pollution, with the increases in these rates paralleling the rise in pollution levels. It, thus, would appear that at every level of pollution, and not at some defined "threshold" depending upon the adaptive reserve of the individual, someone becomes sick and someone's life is shortened. While there may be a biological threshold for tissues, the dose-response relationship, even for individuals, will vary with ageing, acute illness, stress, fatigue, increased physical activity, changes in nutrition, and many other factors. The emergency room and other studies which we also carried out, suggest the possibility that socioeconomic factors may very well be a very significant factor in reducing adaptive capacity. Certainly in a heterogeneous population there is marked dose-response variability and no single population threshold can be defined. It, therefore, follows that definition of the major population groups at high risk and examination of the variation in risk at different pollutant levels represents a reasonable method for examining and predicting health impact on a population. A major weakness in the predictions is the absence of quantifiable data on low level, long term effects of pollutants on health.

Figure VI represents two pathways followed to estimate the health effects of various energy systems. Two examples will be given for quantitating and predicting the health impact of energy consumption.

Pathway "A" represents the steps necessary to define variations in air quality per unit use of energy, which can then be correlated with the biological endpoints. This is summarized briefly in Table V, which shows the fuel consumption in the geographic areas under study. For the example of respiratory disease, pre-school children in cities over 10,000 population with SO_2 levels above 100 mg/m^3 were examined. The estimated total energy consumption in this area approximates 4.1 quadrillion BTU's. For the example estimating excess asthmatic attacks, the City of Chicago data were used. Here the total estimated energy consumption equals 1.2 quads per year.

The human health assessment track is shown in Pathway B, Figure VI. The geographic area to be studied consists of a total population of 21 million people. From a number of studies it has been shown that approxi-

TABLE V

DIFFERENTIAL FUEL CONSUMPTION
IN CHURCHES AND
SCHOOLS

DIFFERENTIAL FUEL CONSUMPTION IN CHURCHES AND SCHOOLS

DIFFERENTIAL FUEL CONSUMPTION (IN GALLONS) OF FUEL AND GAS
IN CHURCHES, SCHOOLS, AND SCHOOLS CORRELATED WITH
SO₂ LEVELS ABOVE 250 $\mu\text{g}/\text{m}^3$

USE	CHURCH	SCHOOL	SCHOOL	CHURCH	TOTAL
CHURCHES AND SCHOOLS	0.1	0.5	0.7	1.3	
SCHOOLS	0.3	0.3	0.9	1.5	
SCHOOLS FUEL CONSUMPTION	0.9	0.1	0.4	1.3	
TOTAL	1.1	1.1	2.0	4.1	

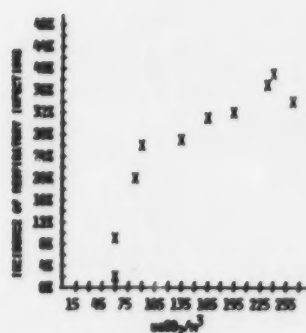
DIFFERENTIAL FUEL CONSUMPTION

DIFFERENTIAL FUEL CONSUMPTION IN CHURCHES - 1.2 GALLONS/YEAR

mately 1.07 million of these are pre-school children. Three studies summarized in Figure VII characterize the change in incidence of acute respiratory disease in children under five correlated with variations in annual SO₂ levels. The results are used to assess the variation in

Figure VII

INCIDENCE OF ACUTE RESPIRATORY DISEASE IN
CHILDREN UNDER 5 CORRELATED WITH ANNUAL
SO₂ LEVELS



- SOURCE: (a) CHURCH, 1973.
(b) J. H. B. CHURCH, S. G. WALLER, JR., J. ENV.
HEALTH, 20(1), 1966.
(c) J. H. B. CHURCH, S. G. WALLER, JR., J. ENV. HEALTH, 20(1), 1966.

morbidity at high and low SO_2 levels. This was found to be 19% (5-24%). Thus, it appears that an excess of 255,000 respiratory infections might occur annually in this population of 1.07 million children under the age of

TABLE VI

PERCENTAGE CONTRIBUTION OF SO_2 TO TOTAL AMBIENT AIR POLLUTION LEVELS BY FUEL AND USE CATEGORIES, 1968, CITIES OVER 10,000 POPULATION WITH SO_2 LEVELS ABOVE $300\mu\text{g}/\text{m}^3$

USE	COAL	OIL	GAS	TOTAL
RESIDENTIAL AND COMMERCIAL	3.2%	13.9%	-	17.4%
INDUSTRIAL	35.8%	1.5%	-	37.3%
ELECTRIC POWER GENERATION	14.8%	1.4%	-	15.4%
TOTALS	53.8%	16.7%	-	70.5%

* NOTE: SIZE OF AMBIENT AIR LEVELS OF POLLUTION ARE DETERMINED TO RESULT FROM ONE-QUARTER SOURCES

five at the higher pollution levels. The number of excess illnesses per quad BTU's of energy can then be estimated when one considers the percentage contribution of SO_2 to total ambient air pollution levels by fuel and use categories. (Table VI) This is summarized in Table VII. An excess of 80,000 respiratory infections results from coal use in this population for residential and commercial, 305,000 from industrial use, 45,000 from electric power generation, with a weighted average for coal of 120,000 excess acute respiratory infections per quadrillion BTU's.

TABLE VII

ESTIMATED EXCESS OF ACUTE RESPIRATORY ILLNESSES
IN 1.07 MILLION CHILDREN 5 YEARS OF AGE
(Total Population 21 Million)

USE	RELATIVE CONTRIBUTION OF FUEL CONTRIBUTING TO AMBIENT SO_2 LEVELS (%)	EFFECT	NUMBER OF CASES PER QUAD			
			COAL	OIL	GAS	WEIGHTED AVERAGE
RESIDENTIAL AND COMMERCIAL	17.4	ACUTE RESPIRATORY DISEASE *	80,000	37,000	-	58,000
INDUSTRIAL	37.3	ACUTE RESPIRATORY DISEASE *	305,000	13,000	-	63,000
ELECTRIC POWER GENERATION	15.4	ACUTE RESPIRATORY DISEASE *	45,000	16,000	-	38,000
WEIGHTED AVERAGE	70.5	ACUTE RESPIRATORY DISEASE *	120,000	36,000	-	46,000

* IN CHILDREN UNDER 5 YEARS OF AGE

** BASED ON RELATIVE CONTRIBUTION OF EACH SOURCE



Figure VIII

Another example examines excess asthma attacks in relation to sulfates. The area defined is the City of Chicago with a population of 3.4 million. In this population, the asthma prevalence rate is conservatively estimated to be 3% for a total of 100,000 asthmatics in the city. The graph in Figure VIII assesses variation of morbidity in samples of asthmatics at varying pollution levels taken from the CHES and Cohen Studies which examined the relationship between sulfate concentrations in the air and excess asthmatic attacks. No excess was found below 7.5 ug/m^3 . An increase in the rate of excess asthmatic attacks per person day, accompanied the increase in sulfate concentration. Figure IX shows the time distribution of airborne sulfate concentration (number of days per year

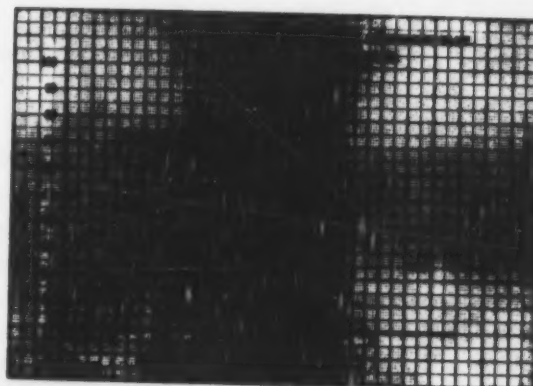


Figure IX

at various concentrations of sulfates for Chicago). An estimate of the quantitative variation in asthmatic attacks at varying levels of sulfate can then be made, using the following formula.

$$\begin{aligned} \text{TOTAL EXCESS} \\ \text{ASTHMATIC ATTACKS} &= A \int_0^{\infty} E(c) \cdot D(c) \, dc \\ &\approx A \sum_{i=1}^n E_i \cdot D_i \Delta C_i \end{aligned}$$

$$\approx 763,000 \text{ EXCESS ATTACKS/YEAR}$$

A = TOTAL NUMBER OF ASTHMATICS IN A COMMUNITY

$E(c)$ = EXCESS ASTHMATIC ATTACKS/PERSON - DAY

$D(c)$ = DISTRIBUTION OF TIME WITH RESPECT TO CONCENTRATION OF AIRBORNE SULFATE

$$\left[\frac{\text{DAYS/YEAR}}{\Delta \text{SULFATE CONCENTRATION}} \right]$$

C = CONCENTRATION OF AIRBORNE SULFATE $\mu\text{g}/\text{M}^3$

From this calculation it would appear in this example that 763,000 excess asthmatic attacks occur per year due to total sulfate exposure. Using the following formula it is suggested that 445,000 excess asthmatic attacks might be expected to occur per quadrillion BTU's of energy from sulfate producing sources.

EXCESS ASTHMATIC ATTACKS X% CONTRIBUTION OF SULFATES

ESTIMATED ENERGY CONSUMPTION

= # EXCESS ASTHMATIC ATTACKS

QUAD

This model can be used to examine other populations at high risk and the variation in risk accompanying a change in the environmental quality. A better definition of those segments of the population at high risk and more sophisticated studies measuring variations in health effects of multiple pollutants in cohorts of these people will increase the accuracy of the model. Better measurements of more pollutants to better quantify environmental stressors also increase its accuracy. While reliability of

the model is severely limited because of the data, more adequate measurements of both environmental and biological endpoints will enable studies to be carried out which will more accurately quantitatively assess health impact.

In Conclusion:

1) A Model is suggested for making predictive quantitations of the health impact of changes in energy use with accompanying changes in levels of pollution;

2) The excess numbers of asthmatic attacks, 455,000/quad, and acute respiratory illness in pre-school children, 120,000/quad, which might be expected to occur suggest that increases in energy use may very significantly affect the health of large segments of the population.

3) Studies similar to the one discussed and additional studies of variation in morbidity and mortality to define the effects on high risk groups at low and high levels of pollution permit the introduction of health impact considerations into decision making regarding energy alternatives.

Finally, it must be recognized that infinite growth in energy use in a finite system is not possible. Industrial societies soon will be required to accept a state of energy equilibrium, i.e. the new use of a quantum of energy to serve an important societal need will require the phasing out of an old use, considered less important and less necessary.

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L'EVALUATION DU RISQUE POUR LA SANTE DE LA POPULATION EXPOSEE AUX POLLUANTS ATMOSPHERIQUES IRRITANTS. ASPECTS METHODOLOGIQUES

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RESUME

Les recherches épidémiologiques effectuées dans des localités à atmosphère polluée par des agents irritants (suspensions et dioxyde de soufre) ont permis l'estimation de la valeur de la sensibilité de certaines méthodes appliquées dans les études sur la population, dans les conditions où le niveau de pollution de l'air n'est pas trop élevé.

Des méthodes utilisées, la corrélation statistique de la morbidité et de la mortalité de la population s'est avérée moins sensible que la comparaison statistique des territoires pollués et non pollués. De même les études effectuées sur des groupes de population à sensibilité accrue envers l'action des polluants irritants se sont avérées d'une plus grande valeur que l'analyse de la mortalité et de la morbidité de la population entière.

Nous avons obtenu ainsi des résultats concluants par l'étude de la prévalence de la bronchite chronique et des symptômes respiratoires chez la population adulte, à l'âge de risque (40-60 ans). Dans le cas de l'investigation de l'action de la pollution atmosphérique sur la santé des enfants, les résultats les meilleurs nous les avons obtenus chez le groupe d'âge de 8-11 ans. Les tests épidémiologiques utilisés chez ce groupe d'âge ont été: l'étude des causes de l'absentéisme scolaire, la prévalence des

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maladies et des symptomes respiratoires, ainsi que l'investigation des modifications de certaines constantes hématologiques.

ABSTRACT

Epidemiological research carried out in localities where the atmosphere is polluted by irritants (suspended matter and sulphur dioxide) has enabled us to estimate the sensitivity of certain methods used for studying the population under conditions in which the level of air pollution is not too high.

Of the methods used, statistical correlation of the morbidity and mortality of the population proved less sensitive than statistical comparison of polluted and non-polluted areas. Similarly, studies carried out on population groups highly sensitive to the effects of irritant pollutants proved of greater value than analysis of the mortality and morbidity of the whole population.

Thus we obtained conclusive results by studying the prevalence of chronic bronchitis and respiratory symptoms in the adult population most at risk (age 40-60). With regard to the study of the effects of atmospheric pollution on child health, our best results were obtained with the 8 - 11 age group. The following epidemiological tests were used for this group: the study of reasons for absence from school, the prevalence of respiratory illnesses and symptoms and the study of variations in certain haematological constants.

Des amples recherches épidémiologiques effectuées dans des localités à atmosphère polluée par des agents irritants, représentées surtout par des suspensions non toxiques comme polluants majeurs et par le bioxyde de soufre et le bioxyde d'azote comme polluants secondaires, nous ont permis l'estimation de la sensibilité de certaines méthodes appliquées dans les études sur la population. Les zones étudiées n'étaient pas soumises à une pollution excessive, fait démontré par l'enregistrement continu des principaux polluants.

Dans ces conditions, les études de corrélation statistique se sont avérées moins sensibles en ce qui concerne l'effet de la pollution de l'air sur la santé de la population, vis-à-vis des études de comparaison statistique, par rapport à une population témoin d'une zone faiblement polluée en respectant évidemment avec rigueur toutes les conditions de sélection correcte des échantillons. Aussi bien, pour les conditions respectives, l'analyse de la morbidité et de la mortalité de la population en général n'a pas réussi à mettre en évidence des effets notables sur la santé, le phénomène étant reflété par l'investigation de l'état de santé de certains groupes de la population à sensibilité accrue envers l'action des polluants atmosphériques.

Dans le cas de l'exposition aux polluants irritants mentionnés on a obtenu la mise en évidence de l'influence sur la santé tant de la population adulte que de la population infantile.

La population adulte la plus sensible s'est avérée le groupe entre 40-60 ans, où on a pu mettre en évidence une fréquence accrue des bronchopathies chroniques non spécifiques et des symptômes respiratoires. Afin de mettre en évidence les malades et les symptomatiques, on a utilisé le questionnaire proposé par le Medical Research Council, avec quelques modifications, et l'investigation de la fonction respiratoire à l'aide de l'expiragraphe Seddani. L'investigation de la fonction respiratoire après l'application des bronchodilatateurs augmente la sensibilité de la méthode. La méthode s'est avérée adéquate à l'étude, mais elle porte

l'empreinte des difficultés techniques (l'interview individuel, le rendement bas de l'examen spirométrique), fait qui rend difficile la poursuite de grands groupes. Compte tenu des difficultés techniques et de la dimension relativement réduite des groupes, l'influence de la pollution sur la prévalence de la bronchite chronique et des symptômes respiratoires est parue plus concluante dans le cas de la poursuite prospective des groupes étudiés.

En ce qui concerne les études sur la population infantile, le groupe le plus sensible s'est avéré celui compris entre 8-11 ans, d'où on obtient une bonne coopération et on évite le risque de l'habitude de fumer comme facteur interférant. Des méthodes utilisées pour la mise en évidence de l'existence de l'influence de la pollution de l'air sur la santé des enfants, l'étude de l'absentéisme scolaire et celui de la fréquence des maladies et des symptômes respiratoires et - en partie - des modifications hématologiques sont celles qui ont donné des résultats concluants.

L'absentéisme scolaire et ses causes ont été étudiées à l'aide d'une fiche individuelle des élèves, qui a été remplie par les cadres didactiques, avec le support de l'infirmière de l'école. Poursuivie assez longtemps, au moins pour une année scolaire, cette fiche a réussi à mettre en évidence certaines particularités de la pathologie des écoliers, les maladies présentant des différences significatives du point de vue statistique étant surtout les affections aiguës et chroniques des voies respiratoires supérieures et du poumon. Les autres causes de maladie n'ont pas présenté de différences entre les zones polluées et les zones témoin, sans pollution. Etant donné qu'il s'agit d'une méthode simple et facile à appliquer, nous la considérons - malgré son manque de spécificité - utile pour apprécier l'effet de la pollution atmosphérique sur la santé.

La fréquence des maladies et des symptômes respiratoires a été étudiée à l'aide d'un questionnaire rempli par les parents et à l'aide de l'examen de la fonction respiratoire chez les enfants des groupes étudiés.

Le questionnaire, comprenant des questions sur les symptômes respiratoires chez les enfants, sur les antécédents pathologiques pulmonaires personnels et hérédocolatéraux, ainsi que sur certaines conditions sociales (le degré d'instruction des parents et les conditions d'habitat, y compris le système de chauffage) ont été remplis en utilisant la méthode de l'interview en groupe (20-30 parents), que nous trouvons supérieure à la méthode de l'interview individuel ou de l'autoadministration. Nous avons préféré cette méthode puisque, en la testant parallèlement aux deux autres, nous avons obtenu un rendement supérieur par comparaison à l'interview individuel, en évitant les erreurs les plus fréquentes observées dans le cas de l'autoadministration. Cette méthode nous a permis aussi l'examen durant le même jour de la fonction respiratoire, en nous permettant ainsi d'obtenir un taux des réponses supérieur (presque 90%). Dans l'investigation de la fonction respiratoire nous avons utilisé la détermination du débit respiratoire maximal, en utilisant le peak-flow-meter Wright, ainsi que la capacité vitale forcée et le débit expiratoire maximal. Pour ces deux mesures nous avons utilisé le vitalographe que nous trouvons satisfaisant en ce qui concerne le rendement et la sensibilité. Afin de simplifier les enregistrements et d'augmenter le rendement, nous sommes en train de tester l'appareil Monaghan aussi.

L'interprétation de ces données comporte certaines difficultés, surtout en ce qui concerne les valeurs normales des fonctions respiratoires, l'établissement des valeurs normales nationales représentant une de nos préoccupations actuelles.

Les examens hématologiques n'ont pas présenté, par leur manque de spécificité, une sensibilité particulière dans l'appréciation des effets de la pollution de l'air sur la santé des enfants. Nous signalons pourtant plusieurs tests hématologiques qui ont indiqué - avec une certaine constance - des différences chez les groupes d'enfants des zones polluées et non polluées, à savoir la quantité d'hémo-

globine des hématies, la fréquence des lymphocytes grands par rapport aux petits, ainsi que la présence des corps toxiques dans les hématies

Nous considérons que l'étude épidémiologique des groupes de population à sensibilité accrue permet l'évaluation des effets de la pollution de l'air sur la santé, même dans des conditions où le niveau de la pollution n'atteint pas de valeurs excessives.

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STUDY ON LONG-TERM EFFECTS ON HEALTH OF AIR POLLUTION

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ABSTRACT

Epidemiological studies are required in order to ascertain the long-term effects on health of exposure to relatively moderate levels of pollution of ambient air.

To avoid the influence of other factors, such as occupational exposure and smoking, studies on children have been recommended.

School children, 8 - 10 years old, living in areas with different levels of air pollution, divided into "highly polluted" (annual median concentration of SO_2 more than $100 \mu g/m^3$ and annual median concentration of standard smoke over $40 \mu g/m^3$) and "low polluted" (SO_2 below $50 \mu g/m^3$; standard smoke below $30 \mu g/m^3$), are investigated by means of a questionnaire filled in by parents or guardians, and by means of lung function tests (Peak Flow Rate, FEV 0.75 and FVC).

Using a common working protocol and reporting forms, studies are currently carried out in five European countries. The results obtained in 1972 and 1973 studies will be analysed by a Working Group to meet in Düsseldorf in April 1974.

1. Introduction

Within the scope of its long-term programme in environmental pollution control, approved by the Regional Committee for Europe of the World Health Organization in 1969 (1,2), the WHO Regional Office for Europe has organized a study on the long-term effects on health of air pollution (3).

The objectives of the study are:

- (1) to investigate the relationship between long-term exposure to air pollution and indices of chronic respiratory disease in children living under different social and domestic circumstances in a number of European countries;
- (2) to evaluate the relationship between air pollution and respiratory disease with a view to providing additional criteria for air quality standards.

2. Method used

While more reliable data were expected to result from a prospective (longitudinal) study, it was decided that, in view of the time and expenditure required for such a study, the prevalence should first be investigated by a cross-sectional study, organized so as to permit a follow-up to be made in a prospective or longitudinal study. The parameters were limited to those thought to be easily quantifiable and comparable.

2.1. Air pollution

While several pollutants have been found to exert adverse influences on health, two pollutants were selected for the purposes of this study, viz. SO₂ and "standard smoke". These have been found to be typical of the reducing type of air pollution in urban areas in Europe, causing or aggravating respiratory symptoms. These are also the pollutants measured most frequently and for the longest period of time. If other pollutants were measured, they could also be recorded and reported.

To guide local teams in the selection of study areas, two levels of pollution were defined:

- (1) High-level pollution: median annual concentration
 $\text{SO}_2 > 100 \text{ mg/m}^3$
and median annual concentration standard
smoke $> 40 \text{ mg/m}^3$
- (2) Low-level pollution: median annual concentration
 $\text{SO}_2 < 50 \text{ mg/m}^3$
and median annual concentration standard
smoke $< 30 \text{ mg/m}^3$

In each country participating in the study, at least two areas, one with high and the other with low pollution, were selected. Since chronic health effects were to be investigated, the air quality records, for at least the previous five years, were thought to be necessary, especially for the areas with high pollution levels.

The methods recommended for SO_2 measurement were the acidimetric hydrogen peroxide method, with automatic sampling and potentiometric titration - OECD (4) - and WHO (5,6,7,) or the West and Gaek colometric method, the former being used as references method if other procedures for SO_2 measurement were employed.

For the determination of standard smoke, the reflectance method (5) was suggested.

The density of the measuring network was to be increased where necessary through the installation of new stations, each area to be covered by at least one station. The frequency of sampling was already determined by the methods of analysis selected, i.e. 24-hourly values for SO_2 and standard smoke. Of great importance was the location of the sampling site, which had to be close to the level of inhalation by the population.

The description of the network, the instruments and methods employed, the tables of all available air quality data, the summary of the data (monthly extreme and mean values) the 90 and 98 percentiles and the median were to be stated.

2.2. Medical and socio-economic data

Schoolchildren 8 to 10 years old were selected as being a fairly susceptible group, generally uniformly exposed to ambient air pollution, not yet affected by smoking and puberty, and no longer under the direct influence of infectious respiratory diseases of early childhood. Children of this age group could also be expected to collaborate well in the pulmonary function tests and their relatively short life span would permit their anamnesis with respect to respiratory afflictions to be rather well established.

The sample proposed for each pollution area was 2000 children, i.e. 4000 for each country (two areas in each country).

To standardize for socio-economic conditions, the educational attainment of the parents and the details of the households were to be recorded (i.e. number of rooms per household, method of heating, number of persons per household.)

Within the study areas, random samples of schools were to be chosen and, within the school classes selected, all children would be investigated. Special schools attended by children, the majority of whom did not live within the study area, were to be excluded.

The studies were conducted in spring, starting almost at the same time and taking about two months.

The personal and medical data were obtained through a self-administered questionnaire and a medical examination of the child.

The questionnaire, accompanied by an explanatory letter, was sent to the parent or guardian who was to provide the personal, socio-economic and health data on the child. These data included information on the presence or otherwise of respiratory symptoms during the previous winter season, the presence of such symptoms in previous years and the child's history with regard to certain respiratory and infectious diseases.

The medical examination yielded, in addition to personal data, information regarding height and weight, the peak respiratory flow rate as measured Wright peak flow meter - (five tests; the flow meters were standardized at the London School of Hygiene and Tropical Medicine), the forced vital capacity (FVC) - (three times, preferably by wet spiograph) and the forced expiratory volume in 0.75 seconds (FEV 0.75).

3. The pilot studies

To test the working protocol for the study, pilot studies were conducted in two countries in 1972, taking one school in an urban district in one country (Denmark), 331 children in the 7-11 year age-group 295 of which completed the investigation and, in another country (Poland), 991 children aged 8-10 years from two schools in a smaller low-level pollution area (monthly means September 1972 - January 1973 at two stations: 5-150 $\mu\text{g}/\text{m}^3$ SO_2 and 40-250 $\mu\text{g}/\text{m}^3$ smoke) and from three schools in a larger high-level pollution area (monthly means September 1972 - January 1973 at two stations: 40-190 $\mu\text{g}/\text{m}^3$ SO_2 - peak >400, and 80-240 $\mu\text{g}/\text{m}^3$ smoke - peak 1200).

Difficulties were encountered with the FVC and FEV measurements, leading to the adoption of the peak flow measurement as the compulsory measurement and the FEV 0.75 and FVC as optional tests.

The study protocol was adjusted accordingly by a working group which discussed the results of the two pilot studies (8).

Contact was established with the Commission of the European Communities in an effort to achieve a common approach to the studies conducted by both organizations and to obtain comparable results.

4. The main study

In 1973, two countries conducted the main studies (Denmark and the Netherlands) and another two started pilot studies (Czechoslovakia and Poland) to test the questionnaire in their particular circumstances. However, since these studies were undertaken using the corrected working protocol and were similar in size and approach to the other main studies, their results are thought to be comparable to the studies conducted in Denmark and the Netherlands and were evaluated accordingly. A fifth country is to conduct the main study in 1974 (Poland).

The Danish study was carried out in spring 1973 on 850 children in a high-class district of the capital (annual means 1971/72: 79/72 $\mu\text{g}/\text{m}^3$ SO_2 and 37/32 $\mu\text{g}/\text{m}^3$ smoke), 1300 children living in a working-class district of the capital (annual means 1971/72: 87/66 $\mu\text{g}/\text{m}^3$ SO_2 and 31/26 $\mu\text{g}/\text{m}^3$ smoke), both at the same levels of air pollution, on 1600 children in a low-pollution urban area (annual means 1972: 28 $\mu\text{g}/\text{m}^3$ smoke) and finally on 800 children in a rural area with very low pollution (annual means 1972: 9 $\mu\text{g}/\text{m}^3$ SO_2 and 7 $\mu\text{g}/\text{m}^3$ smoke). The data which are not yet fully evaluated, do not seem to indicate a clear correlation between prevalence of respiratory diseases and air pollution when results are adjusted for social class differences.

In the Netherlands, 2104 children aged 9-11 years, were investigated in a high-level pollution area (annual means at seven stations: 100-190 $\mu\text{g}/\text{m}^3$ SO_2 and 25-45 $\mu\text{g}/\text{m}^3$ smoke) and 276 in a low-level pollution area (annual mean at one station: 50 $\mu\text{g}/\text{m}^3$ SO_2 and 10 $\mu\text{g}/\text{m}^3$ smoke). A general trend towards higher prevalence of respiratory symptoms was found in the high pollution area, although the findings did not reveal clear and significant differences.

The study in Czechoslovakia was conducted on 4276 children aged 8-11 years in two highly polluted areas (annual mean SO_2 concentration 1969/70/71: 170/130/150 $\mu\text{g}/\text{m}^3$ and 120/140/170 $\mu\text{g}/\text{m}^3$ respectively; estimated mean air-borne dust aerosol in 1970: 109 and 170 $\mu\text{g}/\text{m}^3$ respectively), and in four less polluted areas (annual mean SO_2 concentration for 1972: 40/80/106/75 $\mu\text{g}/\text{m}^3$ respectively; estimated air-borne dust aerosol in 1970 - not stated/76/105/99 $\mu\text{g}/\text{m}^3$ respectively). Preliminary analysis shows significant differences in the prevalence of respiratory symptoms as between high-level and low-level pollution areas.

The study conducted in Romania in 1973 yielded preliminary indications of a higher prevalence of respiratory symptoms in a high-level pollution area (1974 children) as compared with a low-level pollution area (1918 children).

5. Evaluation

A numerical evaluation of the study results is at present underway, and a preliminary assessment (9) of the results has shown that the trends observed will be established more clearly by a longitudinal (prospective) study which is being set up for the next three to five years.

The cross-sectional study showed that methods and equipment have to be closely standardized to exclude experimental bias. While this appears to be easier for the medical part of the study, if the peak flow rate is taken as the significant measurement, no comparison is possible between countries in respect of air quality measurements obtained. Although air pollution levels in the various study areas within a country can be compared, standardized equipment will have to be provided to make valid inter-country comparison possible. This should go hand in hand with the training of equipment operators.

During the cross-sectional study all Wright peak flow meters were calibrated at one place (London School of Hygiene and Tropical Medicine), whereas no air quality measurement

equipment was calibrated. However, even with the calibrated flow meter, the questionnaire replies to questions on respiratory symptoms seem to yield more conclusive answers than the measured expiration values in relation to levels of air pollution.

In international study special attention had to be paid to language problems. Since the standard questionnaire had been prepared in English and was to be used in the local language, the correctness of the translation into the local language was checked by having it re-translated into English by a translator not connected with the study. In spite of this precaution, 4 questions were consistently replied to in an unexpected way in one of the study areas.

Consultants visited the various pilot areas during or after the studies. It is planned to organize such visits before and during the longitudinal study.

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PANEL DISCUSSION

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SUMMARY OF THE DISCUSSION

This panel, chaired by F.G. Hueter, addressed itself to the subject of evaluation of health risks of populations exposed to irritant atmospheric pollutants. The emphasis in this regard was on the methodologic aspects of these human population studies.

The chairman initiated the discussion period by identifying two major considerations which had come to light through the formal presentations:

- one consistent thread through the formal presentations was the use of health questionnaires and respiratory function studies to elicit human health effects data. The chairman questioned the relative importance of developing and applying other non-respiratory and more sensitive biologic parameters for the assessment of adverse air pollution health effects;
- another consideration which was highlighted during the formal presentations was the importance of the sub-groups used in population studies. Selecting appropriate, susceptible, populations bears directly on the validity and applicability of the resultant data.

There was general agreement among panel members that the epidemiologic study, as a methodologic approach to the assessment of air pollution effects, has been perfected to the point that the variables employed can be very carefully controlled. In a discussion of populations to be considered, for instance, the group agreed that special populations, such as survival populations, can be identified and avoided at the outset for a given study.

The group recognized that there is still an insufficient data base for making decisions on air pollution control, and, in

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comparability in human population studies. If standardized methodologies can be developed and applied, then data from many different countries can be correlated to provide a firmer data base. The group also recognized that for certain types of studies, world-wide uniformity of methodology is not now feasible. Because of such factors as socio-cultural orientation, differences in nutrition, differences in genetics, and the like, certain populations cannot be compared.

A second general consensus was that the effort towards comparability can be enhanced considerably by international cooperative studies. It was agreed that such a pooling of expertise could result in great strides in the control of air pollution.

DISCUSSION

HUETER (U.S.A.)

A number of the presentations have contained a thread of continuity, but, on the other hand, there have been obvious differences in experimental approaches used by various investigators. Time does not allow a discussion of all these differences, but I feel that there are two major areas which the panel could address. One of them is that most reports concern the health questionnaires and respiratory function measurements. Several reports also included hematological and enzymatic, bacteriological type of data. I would like the panel to consider what is the importance of developing and/or applying non-respiratory or other more sensitive biological parameters for assessing both qualitatively and quantitatively the adverse

health effects from exposure to air pollutants. The second point is that various investigators have studied health effects using different subgroups of the population. The question is, "what are the most appropriate susceptible populations to study for discerning and quantifying adverse health effects of air pollution". I would like to request Dr. Carnow to begin the discussion on the aspect of questionnaires and respiratory function.

CARNOW (U.S.A.)

Everybody is very defensive about questionnaires and I would like to raise the question concerning more sensitive parameters. We used questionnaires to define the levels of inadequacy and disease of 560 bronchitics in the City of Chicago. We followed these people for some five years and our data have been published. In relation to the integrity of the questionnaires, we carried out some validation studies and found a number of interesting things. There were very high positive correlations between the dyspnea index (developed by the British), the cough-phlegm index, frequency of past history of illness index, and spirometry. We also found a very high correlation with subsequent mortality, in that 80% of all deaths were cardio-respiratory and most occurred in those we had classified as Group 4 - severe bronchitics. Classification was based solely on information from the questionnaires. Thus, questionnaires appear to be at least an important prognostic and, perhaps, a diagnostic tool.

There is more regarding the validity of questionnaires. We analyzed 36 months of data and found that those people who, in the initial questioning, said that they were sensitive to high humidity, indeed proved to be sensitive. There was a significant relationship between their illness over the 36 months and days of the highest humidity. Those who said they were sensitive to heat appeared to be more sensitive and had more

illness episodes related to heat. Those who reported that they suffered from frequent respiratory illness, were found to have a much higher frequency of respiratory illnesses.

In many ways, I think people know about their environmental sensitivities. Responses to questionnaires can be extremely valuable if they are standardized and if personal questions are not included by the questioners; who must be trained for a short period of time to ask standard primary and secondary questions. In summary, I think that questionnaires should not be thought of as crude or of little value. They are a very good way to obtain data.

SCHMIDT (CSSR)

Wir haben heute zum Thema Asthma und ins besondere zum Problem der auslösenden Faktoren zahlreiche Beiträge gehört. Eine weitere Möglichkeit in diesem Zusammenhang bietet die Ueberwachung des Arzneimittelvebrauchs. Bekanntlich besteht in unserem Land ein zentralisierter Gesundheitsdienst, was dem Kollegen Hruby aus Brunn die Möglichkeit gab, den Verbrauch von Antiasthmatica in Regionen mit starken und relativ geringer Umweltverschmutzung zu vergleichen. Dabei zeigte sich, dass der Verbrauch in den verschmutzten Gebieten höher war.

In der Frage, welche Kriterien bei Untersuchungen von Kindern oder anderen Bevölkerungsgruppen am besten zugrunde zu legen sind, sowie in der Frage der Bedeutung der sich aus Lungenfunktionsprüfungen, epidemiologischen Fragebogenaktionen und spezifischen Kinderuntersuchungen ergeben den Abweichungen bei anderen biologischen Parametern vertreten wir die Ansicht, dass die meisten oder alle unsere Befunde physiologischer Art sind. Es handelt sich also nicht um pathologische Veränderungen. Die festgestellten Veränderungen führen jedoch zu der Erkenntnis, dass der Organismus des Erwachsenen bzw. des Kindes

einen Langzeitstress ausgesetzt ist. Die Frage, welche Altersgruppe sich am besten für Untersuchungen eignet, ist, wenn es sich um Untersuchungen auf der Grundlage von Anamnesen oder Fragebogen handelt, nicht von großer Bedeutung; werden jedoch gezielte klinische und Laboruntersuchungen durchgeführt, dann halten wir aus folgenden Gründen die Altersgruppe zwischen 7 und 12 Jahren für die geeignetste:

1. Kinder haben zwangsläufig bereits gewisse Zeit unter bestimmten Bedingungen gelebt, d.h. entweder in einer Region mit oder ohne Umweltverschmutzung.
2. Kinder arbeiten bei den Untersuchungen willig mit.
3. Kinder rauchen nicht, trinken keinen Alkohol und halten sich nicht am einem Arbeitsplatz auf, so dass einige der zahlreichen Fremdfaktoren ausscheiden. Auch spielen in diesem Alter die Pubertätsakzelerationsfaktoren noch keine Rolle.

With reference to the contributing factors, a lot has been said about asthma at this Symposium. There is yet another possibility and this is to observe the use of drugs. The centralized health service network in our country, enabled Hruby, from Brno, to compare the use of asthma drugs in polluted and relatively unpolluted areas. The investigation showed that they were used more in exposed areas.

Turning to the question of the best criteria to use for surveys of children or of the general population, and to the significance of the variations in other biological parameters which have emerged from lung tests, epidemiological questionnaires and specific child surveys, we find that the majority of, or all our findings, are physiological in nature; we are not dealing with pathological changes. However, the changes found indicate that the adult's or child's organism has to fight against long-term stress and this is important. Which age group do we consider most suitable for the survey? This is not so important for surveys based on case histories or questionnaires but when the survey has specific objectives and is carried out clinically and in the laboratory, we consider the age group from 7 to 12 years to be the best for the following reasons:

1. *children have already been obliged to live in a given environment for a certain period of time, i.e. in a polluted or unpolluted area;*
2. *children are cooperative.*
3. *children do not smoke or drink and do not spend their time at a place of work, which means that we can eliminate some of the many extraneous factors; children of this age are not yet affected by factors arising at puberty.*

BRILLE Mme (France)

Pour répondre à cette question, il faut lier deux des points que vous avez indiqués, le choix des différentes populations d'une part et d'autre part s'il faut étudier les effets de la pollution à long terme, ou s'il faut au contraire étudier les effets courts, aigus, subaigus, car le choix de la population dépend du type d'étude que l'on veut faire. D'après ce qui est déjà connu par des études épidémiologiques et à la suite de constatations cliniques, les effets aigus sont particulièrement bien étudiés sur certaines populations susceptibles faites de vieillards, de malades respiratoires ou cardio-respiratoires déjà connus et d'enfants très jeunes, de nourrissons. Là, je crois qu'il n'y a pas de doute que pour les effets aigus, il faut étudier des populations susceptibles. Ce choix repose aussi sur le résultat d'études expérimentales faites chez l'homme, comme par exemple, celles qui ont été faites à l'Unité de Recherche "Pollution Atmosphérique" de Londres, par Waller, qui en parlerait mieux que moi. Ces études ont montré que si l'on expose des sujets normaux à des concentrations de polluants atmosphériques bien supérieures à celles que l'on trouve dans l'atmosphère, en particulier pour le SO_2 , on n'arrive pas à provoquer de symptômes ni même de modifications plus fines, comme celles de l'augmentation des résistances de voies aériennes, sauf dans quelques cas et en utilisant des taux énormes qui n'ont strictement rien à voir avec les conditions rencontrées

dans l'air ambiant. Dans ce type d'expérience on n'obtient de réactions que si l'on étudie des sujets asthmatiques ou ayant une réponse positive à un test à l'acéthylcholine, c'est à dire une hyperexcitabilité broncho-motrice: on peut alors obtenir des augmentations de résistance en les exposant à des taux voisins de la pollution atmosphérique générale.

En ce qui concerne l'étude des effets chroniques à long terme, le choix de la population n'est pas aussi clair et il est actuellement l'objet de discussions. On peut dire qu'il y a actuellement deux attitudes: l'une, de n'étudier que des enfants et je pense que ce choix sera défendu par Irwig, et l'autre qui consiste à ne pas se limiter aux enfants, mais à étudier des adultes. C'est l'attitude que nous avons choisie après une discussion de tous les responsables de notre étude en France, appuyée sur les données de la littérature. Je rappelle les avantages d'une étude d'enfants d'âge scolaire: ils ne fument pas, ils restent toute la journée dans la zone où ils habitent (les mesures de pollution atmosphérique de cette zone sont donc représentatives de ce à quoi ils sont soumis) et ils n'ont pas d'exposition professionnelle; en outre à cet âge un test peut être fait pour mesurer la fonction pulmonaire. Je pense cependant qu'il y a deux inconvénients à n'étudier que des enfants: l'un est que nous ne pouvons pas affirmer que la susceptibilité des voies aériennes d'un enfant sont les témoins exacts de la susceptibilité des voies aériennes d'un adulte. L'autre inconvénient découle de l'effet additif possible, peut-être même plus qu'additif, de plusieurs irritants; à ce point de vue il est possible que l'on mette plus facilement en évidence l'effet de la pollution atmosphérique chez les fumeurs que chez les sujets non fumeurs; ceci apparaît dans des études comme celle de Lambert et Reid en Grande Bretagne.

Dans le même ordre d'idées, on peut penser que les ouvriers soumis à une exposition professionnelle ont des voies aériennes plus susceptibles de réagir à la pollution atmosphérique. Une étude des effets de la pollution atmosphérique dans la

population ouvrière pourrait donc être fructueuse, mais pour être valable, elle devrait absolument comprendre une étude détaillée des postes de travail, avec entre autres, des mesures de l'atmosphère du lieu de travail. Ainsi que je l'ai dit précédemment, l'exposition professionnelle est très diverse et est beaucoup plus difficile à prendre en compte dans l'analyse que la consommation de tabac. C'est pourquoi il nous a paru raisonnable, tout en le regrettant, de limiter notre étude aux autres catégories socio-professionnelles.

L'âge des adultes à étudier mérite aussi discussion et l'on doit ajouter les raisons qui, dans notre étude, ont conduit à retenir les sujets âgés de 25 à 59 ans: à côté de problèmes de croissance, les jeunes adultes sont rarement stables quant à leur domicile (et à ce point de vue les sujets de plus de 60 ans, du fait de la cessation d'activité leur ressemblent) il a donc paru déraisonnable de les étudier dans une étude d'effets à long terme ou l'on souhaite une résidence d'au moins trois ans dans la zone étudiée. En ce qui concerne les sujets âgés de 60 ans et plus, la pathologie respiratoire est chez eux trop fréquente par l'accumulation de nombreux facteurs étiologiques et trop souvent intriquée à d'autres maladies pouvant retentir sur la fonction pulmonaire, pour pouvoir être considérée comme un "réacteur" à la pollution atmosphérique.

Pour l'étude coopérative française, il a donc été décidé d'étudier à la fois les enfants de 6 à 10 ans, et les adultes de 25 à 59 ans pour les raisons que je viens de donner; mais je serais très intéressée de savoir s'il y a d'autres arguments en plus de ceux qui ont déjà été développés, en faveur du choix de telle ou telle population pour l'étude des effets à long terme.

In order to answer that question, the two points to which you have referred should be taken together; on the one hand the populations to be selected and on the other the question whether the long-term effects or the short-term, acute and sub-acute effects of pollution should be studied, for the choice of

population depends on the type of survey one has in mind. According to the information already obtained from epidemiological studies and clinical observation, the acute effects have been subjected to thorough examination on certain sensitive populations consisting of old persons, persons in whom respiratory or cardio-respiratory disease has already been diagnosed and very young children, infants. I think there can be no doubt that, in dealing with acute effects, sensitive populations should be studied. This choice is also based on the result of experimental studies made in man such as, for example, those carried out in the "Atmospheric Pollution" research unit in London by Mr. Waller, who is better able than I to discuss them. These studies show that, if normal subjects are exposed to levels of atmospheric pollution greatly in excess of those found in the atmosphere, in particular of SO_2 , it is not possible to produce symptoms, nor even minor changes such as increased resistance of the air passages, except in a few cases and by using very high concentrations which have nothing in common with the conditions in the ambient atmosphere. In this type of experiment, reactions are obtained only if the subjects studied are asthmatic or have a positive response to an acetylcholine test, i.e., if they suffer from broncho-motor hyperexcitability: it is then possible to obtain increased resistance by exposing them to concentrations close to those found in general atmospheric pollution.

With reference to the study of chronic long-term effects, the choice of population is not so obvious and it is at present the subject of discussion. It is fair to say that, at present, there are two points of view: one, that only children should be included in the survey - a choice which I think Dr. Irwig would support - and the other, which consists in not limiting the survey to children but in including adults as well. This is the policy which we have adopted after a discussion, based on the information in the literature, with all those in charge of our survey in France. I would again point out the advantages of a survey of children of school age: they do not smoke, they spend the entire day in the zone where they live (the atmospheric pollution readings for that zone are therefore representative of the pollution to which they are subjected) and in their case there is no occupational exposure; besides, at that age a test can be carried out to measure pulmonary function. I think however that there are two disadvantages in restricting the survey to children: the first is that we cannot be sure that the sensitivity of a child's air passages coincide exactly with that found in an adult. The other disadvantage stems from the possible additive effect, perhaps even more than additive, of several irritants; from this point of view it is possible that the effects of atmospheric pollution can be demonstrated more easily in smokers than in non-smokers; this is clear in studies such as those by Lambert and Reid in the United Kingdom.

By the same token, one might think that the air passages of workers subjected to occupational exposure are more sensitive to atmospheric pollution. A study of the effects of atmospheric pollution in the working population might therefore be useful, but in order to be worthwhile, it would have to include a detailed study of workplaces with, *inter alia*, measurements of the local atmosphere. As I have already said, occupational exposure is very varied and much more difficult to take account of in the analysis than tobacco consumption. For that reason, we reluctantly concluded that it was better to limit our survey to the other socio-professional categories.

The age of the adults to be included in the survey should also be considered and we must therefore give the reasons why we selected subjects aged between 25 and 59: apart from problems of growth, young adults seldom live for long in the same place (and in this respect, persons over 60 years of age, when they retire, resemble them), so it seemed inadvisable to include them in a survey of long-term effects for which residence of at least three years in the zone surveyed is desirable. In persons over 60, the frequent instances of respiratory disorders are too often due to the accumulation of numerous etiological factors, and too often linked with other diseases liable to affect pulmonary function, for them to be seen as a "reaction" to atmospheric pollution.

For the combined French survey, it was therefore decided to use children from 6 to 10 years old and also adults from 25 to 59, for the reasons I have just explained: but I should be very interested to know if there are other arguments, in addition to those which have been put forward, in favour of selecting any given population for a survey of long-term effects.

IRWIG (U.K.)

Basically I do not disagree with Dr. Brille. As in all epidemiological studies, the population that one should be looking at, should be chosen in terms of the question that is being asked. If one wishes to use populations as an indicator of the biological effects of pollution, for example if one wanted to compare the relative effects of smoke and SO₂, it would seem reasonable to choose that population which was sensitive to the pollutants under study, which was easy to obtain, and in which there were minimal other interfering factors. It seems that there is a fair amount of consensus that the childhood

population forms such a group. If on the other hand, one wishes to take on the enormous task of estimating the potential benefits of improvement of environmental pollution levels, then one has to study all the population groups and all changes in health status within those populations. So if one wanted to compare, the cost of improving air pollution levels with the benefit obtained, then it would be necessary to have a look at all population subgroups within that community.

KNELSON (U.S.A.)

I believe the two questions our colleagues have been addressing in the last few minutes are inextricably intertwined. The choice of health parameters as a means of exploring the relationships between environmental stress and the health status of population, as well as choosing the subsets within that population cannot be discussed separately. There are some interrelationships between the two. I agree and certainly I think it has been well demonstrated by virtue of our experience with the rather clear cut results of major catastrophic episodes of the last couple of decades that the very young, the very old and infirm, as we always say in our manuscripts, are those that are most susceptible; but, in what way? Of course, in these catastrophic episodes, we were observing largely excess mortality, as well as excess overt morbidity. As we attempt to delineate in somewhat more detail and more refined fashion, the relationships that we are exploring here, I think we need to look carefully at other tools and to what subsets of the population these tools may be amenable. We have concentrated, as has been the experience of all the people on the panel, primarily on pulmonary disease. Most of us, historically, have been associated with air pollution health effects studies and obviously, the lung and the respiratory tract in general is the organ of insult. The lung constitutes the greatest interface between man and his environment so it

is always a logical organ to explore. But I think we must not be narrow-minded in continuing to slice thinner and thinner and explore in more and more detail the relationships between air pollution and lung function at the expense of other health effects and at the expense of susceptible population sub-groups other than the young and the old and the infirm. We have in our laboratories in the U.S. Environmental Protection Agency begun to use in population studies the tools that are developed in clinical laboratories. As we have begun to design our population studies with this in mind, it has given us an opportunity to enlarge the scope of our investigation where we are no longer limiting ourselves to the classic cardio-pulmonary kind of examinations. I agree wholeheartedly with Dr. Carnow that the continued use of questionnaires is a very valid tool and I am reassured by his experience that the large investment we are making in this kind of health indicator is likely to continue to pay off as it has in the past. However, there are specific areas that deserve more attention, and we are using our experience in the clinical laboratory now to design experiments with populations to explore, for example, cytogenetic effects - we only recently have the tools to do that - and to explore the immune status of populations. We know from questionnaires that one of the most reliable indicators of health effects of environmental stress is an excess of respiratory tract infection of a variety of kinds. However, what are the effects on the more subtle parameters of immune status in the populations that do not overtly express the environmental insult with lung disease or respiratory disease and how is their immune status altered so that other infectious diseases are allowed to manifest themselves? We have recently begun to learn about the whole field of carcinoma-associated antigens, and we already have some preliminary evidence that environmental insult is somehow involved in the whole story of these carcinoma-associated antigens. These are offered simply as examples of how I believe the investigators who are designing the clinical as well as the

epidemiologic studies should broaden their scope both with respect to the tools that they use and the populations in which they use them.

KUMPF (W.H.O.)

I would only like to mention for international studies, perhaps some practical points, that is the accessibility of the study population, the feasibility of the study including the cost and if it is decided to study respiratory affliction, it may be that school children are not the most susceptible group, but certainly they are accessible and the cost of the study can be kept rather low using school health examination. This has been a major factor in determining the age group in our study.

In addition, school children of the age groups selected, i.e. from 8 to 10 years, have as a study group all the advantages mentioned already by Dr. Schmidt, i.e. they are not yet affected by smoking and puberty, are fairly uniformly exposed to air pollution, especially if the school is located in the neighbourhood where the children live, as would be expected with elementary schools for that age group; they are expected to collaborate well with the pulmonary function tests and can be followed up later.

HUETER (U.S.A.)

How much stress should be placed on the air pollution measurements?

BOURDEAU (C.E.C.)

I think this is a point which has been brought out indirectly, at least by the report we heard on the WHO study.

The measurement of independent variables is of course of capital importance in drawing conclusions from epidemiological surveys and we ought to try to avoid the pitfalls that have affected previous studies by trying to make those air pollution measurements as comparable as possible. Special emphasis has been placed on this point in organizing the European Community survey. The SO_2 measurements may be considered to be fairly comparable. The problem of particulates is more complex since in some countries they are measured as smoke, in others by gravimetric methods. Moreover, it has been shown by the very interesting studies from the CHES programme, that quite possibly sulphates will show closer relationship with respiratory effects than any other parameters of air pollution. Considerable thought will be given to that in the implementation of the European Communities' study.

HUETER (U.S.A.)

Closing the discussion between panel members, the panel is now opened to questions from the floor.

ZIELHUIS (Netherlands)

1. International studies conducted by EEC and by WHO - Europe have been discussed. It is not a waste of manpower and money if within Europe both studies are conducted at the same time?
2. Drs. Bourdeau, Brille, Kumpf and Knelson spoke about annual average levels for SO_2 etc. However, 24 hrs. levels usually are distributed according to log-probability scale. Should exposure data be studied according to the specific annual distribution?
3. International comparison assumes similar dose-response relationships. However differences between countries exist in

- genetics, e.g. alpha-antitrypsin deficiency
- socio cultural factors, determining the subjective interpretation of e.g. irritation
- nutrition status (quantitative, qualitative, e.g. milk, protein intake) may determine susceptibility.

So, international comparability is only possible if all the covariables are taken into account. Is this done in EEC and WHO studies?

4. Dr. Carnow proposed a predictive model. He stressed the effect of socio-economic status on susceptibility. This prediction of excess bronchitis/asthma per increase of energy consumption assumes no change in socio-economic status. This prediction strongly supports a change in socio-economic politics.

KUMPF (W.H.O.)

Mr. Chairman, I could perhaps try to reply to two of the questions:

There is a difference in the area covered by the 2 studies as the European region of WHO extends much beyond the nine member states of the European Community. However, the method of approach is similar with the main difference that WHO uses a mailed questionnaire whereas CEC uses one administered by interview.

CEC has participated in all or most of the meetings of WHO on this study, and of course CEC, in a way is in a position to profit from the results of the WHO study. The WHO study will have to be tightened up as far as the air quality measurements are concerned, hopefully with the collaboration of CEC.

Differences in nutritional status between the various national groups are not being considered in the study, however, differences in socio-economic conditions are summarized in the information of the living conditions of the family of the child and the educational level of the parents. These seemed to be the only parameters which could easily be determined in the various countries under the different socio-economic conditions.

BOURDEAU (C.E.C.)

I can say very little in addition to what Dr. Kumpf has said. The two studies are coordinated and should yield more information than the sum of two isolated studies; concerning the non-environmental link or non-air pollution link differences between populations, an attempt was made to get at that by having in each country zones of low pollution and zones of fairly high pollution either in SO_2 or particulates, wherever available.

Regarding the use of annual concentrations whereas we have a log-probability scale, his, of course is a point but we have not only the average annual concentrations. These are used actually to select the areas, but afterwards, winter concentrations, monthly concentrations, and even daily average concentrations will be available which might be used in the analysis of the data, if needed.

CARNOW (U.S.A.)

Concerning Dr. Zielhuis' comment that the prediction strongly supports a change in socio-economic politics. This is true, and is, of course, one of the values of prediction. No matter how crude it is, it gives us some opportunity to vary alternatives so that in looking at energy we can consider low, moderate, or high scenarios and, as I said, try to structure

a more rational energy program based on that. The way we are doing it now is to react to emergency situations and the solutions are frequently worse than the problems that were originally present. In addition, these models are completely flexible and can be modified as time goes on. As variables change, new data can be added to the model (i.e., new epidemiological data on quantitation of biological responses or the finding of new risk populations).

As we become more sophisticated in our environmental modeling (i.e., better diffusion models and monitoring equipment) one can add these also. By the way, for SO_2 and the pollutants we measured, 15-minute values were used, from which we derived 24-hour averages at each station. They were not annual averages nor were they citywide. I think citywide or annual averages are generally inadequate as estimators of population exposure.

We not only used individual 15-minute values at each station, but we developed a linear model using all the stations and an infinite number of data points to estimate square mile values for each 15-minute of each day for 36 months in order to estimate exposures of the 560 bronchitics monitored for illness in one of our studies.

KARHAUSEN (C.E.C.)

If lower respiratory disorders like emphysema, and asthma have a strong genetic component and if the geographic distribution of the genetically susceptible individual is not homogeneous (as indicated by the results of the WHO study in Roumania), the results of those studies might not be about the sole relationship between environmental factors and respiratory illness but actually between genetic factors, environmental factors and respiratory disorders.

CARNOW (U.S.A.)

You are talking about national group characteristics or genetic or ethnic factors which may be important in disease. I think there is something that is very important in what you are saying. I do not know if you meant this also. but there is frequently self-selection of populations and I think that considerable caution should be exercised because of this.

In the United States greater numbers of people die from emphysema in Arizona and Idaho, states that generally have little pollution, than in other states. I think that those families that can afford to relocate may leave an area of high pollution because they have children who have frequent respiratory illnesses. Those remaining in the highly polluted areas may be non-pollution sensitive (i.e. no asthma, allergies, alpha anti-trypsin deficiency, etc.) so you may be dealing with a survival population. Just briefly, we looked at a group of octogenarians in Chicago and found that they were very resistant to pollution. They had lived in Chicago for 65 years, were generally non-smokers, had no history of respiratory disease, and had survived everything Chicago had to offer. They were a survival population who are very resistant and draw general conclusions regarding the effects of pollutants on people in general.

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N.K. WEAVER (U.S.A.)

TOXICOLOGIC ASSESSMENT OF THE HEALTH EFFECT OF SULPHUR
DIOXIDE AND SULFATE PARTICULATES

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ABSTRACT (*reduced by the Editorial Board*)

The health effects of particulates in the inhalation of sulfur dioxide and other gases has not yet been satisfactorily defined. It is known that several factors contribute to the biological response elicited when particles and gases are inhaled. Among these are the size of the particle, its shape, the concentration of particles in the gas medium, and the physio-chemical properties of the particulate, especially its reactivity with components of the gaseous phase and its solvent action related to the gaseous phase.

While sulfur dioxide in sufficient concentration is a respiratory irritant, it rarely, if ever, occurs at irritation concentrations in the urban environment even in "episodes." It has become, therefore, a so-called "index of pollution" and not a cause per se of health consequences.

On these grounds it then becomes important to examine the health effects of the particulate matter dispersed in the urban air, notably, particulate sulfate aerosols which result from catalytic oxidation of the sulfur dioxide effluent from stationary power sources, or from catalytic converters employed to reduce carbon monoxide and hydrocarbone emissions from mobile sources of pollutants.

The study described in this paper on the particulate, obtained by high-volume sampling from four coal-burning plants in

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the Eastern United States disclosed no injurious effects when particulate of <5 microns in diameter was inhaled by monkeys for 18 months, 22 hours a day, at concentrations of 100 or 500 $\mu\text{g}/\text{m}^3$.

In spite of the lack of apparent injurious effects from sulfur dioxide in the long-term studies cited above, it has been shown by Amdur and Underhill (*Arch. Environ. Health* 16:480 (1968) that sodium chloride aerosol ($10 \text{ mg}/\text{m}^3$) exacerbates the irritancy properties of sulfur dioxide (2 ppm) as determined by increased pulmonary flow resistance following single, one-hour exposures of guinea pigs. The authors infer from these data that the resistance to airflow through the respiratory tract is a function of the solubility of sulfur dioxide in the particulate aerosol.

Further information has been developed which suggests that the irritant properties of sulfur dioxide might not only be enhanced by its solubility in a particulate phase but also by its subsequent oxidation to sulfuric acid. Preliminary studies by Amdur and Underhill (*vide infra*) have shown that insoluble, solid aerosols, such as carbon, manganese dioxide, fly ash, triphenylphosphate, and iron oxide, were inactive in potentiating the irritant effect of sulfur dioxide in guinea pigs exposed for one hour. However, soluble, solid aerosols, such as manganese chloride, sodium orthovanadate, and ferrous sulfate, all significantly potentiated the irritant property of sulfur dioxide.

It is evident from these toxicologic data that not all airborne contaminants potentiate the irritant action of sulfur dioxide in single exposures, but that potentiation of toxic effects is dependent on the ambient catalysis of sulfur dioxide and SO_2 = and the latter on the oxidizing capacity of the catalytic aerosol. Many sulfates in aerosol form possess far greater toxicologic activities than sulfur dioxide. The health consequences of the conversion of sulfur dioxide to sulfate either in the atmosphere or as a result of the oxidation of sulfur in fuels by catalytic converters demand increased research before an adequate margin of safety can be defined for sulfate emissions.

In the assessment of the effects on human health resulting from exposure to environmental contaminants, the data base derived from human experience is seldom adequate to make sound judgments as to the deleterious or beneficial effects on humans of any substance or group of substances. Therefore, the standard setting process employed by a regulatory agency to control exposures to pollutants is hampered by the limitations of the health intelligence requisite to the establishing of a scientifically defensible standard.

On the other hand, even when substantial human data are available on a particular pollutant, there is seldom a consensus on the meaning or significance of this information especially with respect to an environmental standard.

While it may be held that the best way to study man is to study men themselves, significant limitations inhere in the use of people for the assessment of health effects.

Animal studies, too, are limited. The central issue herein is whether the pollutant, in effective quantities, gains access to the site of action. Species or strain variations, differences from man in the absorption, distribution, metabolism, and excretion inveigh against the easy acceptance that any animal provides valid clues for examination of effects of the same agent on human. Therefore, biochemical and toxicologic similarities between animals and man should be elucidated before the animal model can be satisfactorily employed to quantify the human response to an environmental pollutant. If the ideal were possible, animal studies to define relative toxicity should be followed by low-dose metabolic studies in healthy humans, and then a representative animal model should be sought so that definitive biochemical, pharmacologic, and chronic toxicologic studies can be performed.

Considering the toxicology of sulfur dioxide and sulfate compounds or the so-called sulfates, animal experiments yield data applicable to man because of the similarity of response to the single agents. However, the health effects of particulates

combined with sulfur dioxide or sulfates has not yet been satisfactorily defined.

It has been shown by Amdur and Underhill (Arch. Environ. Health 16-460 1968) that sodium chloride aerosol (10 mg/m³) exacerbates the irritancy properties of 2ppm sulfur dioxide as determined by increased pulmonary flow resistance in guinea pigs following single, one-hour exposure. Furthermore, aerosols of other salts, for example, potassium chloride and ammonium thiocyanate, in which sulfur dioxide is more readily soluble, produced a greater enhancement of the irritant effect than equivalent air concentrations of sodium chloride.

Further information has been developed which suggests that the irritant properties of sulfur dioxide might not only be enhanced by its solubility in a particulate phase but also by its subsequent oxidation to sulfuric acid. Preliminary studies by Amdur and Underhill (vide infra) have shown that insoluble, solid aerosols, such as manganese chloride, sodium orthovanadate, and ferrous sulfate, all significantly potentiated the irritant capacity of sulfur dioxide.

Long-term inhalation studies employing guinea pigs and monkeys exposed to sulfur dioxide, particulate matter, and sulfuric acid aerosols elucidate their biologic action. Exposure times were 22-23 hours a day for one year in guinea pigs and 1.5 years in monkeys. Guinea pigs inhaling 250, 2,500, or 13,000 ug/m³ exhibited no deleterious effects as judged by survival, body weight, hematology, clinical biochemistry, respiratory function, or pathology.

As illustrated in Table I, an exposure level of 13,000 ug/m³ was associated with increased lung diffusion, reduced lung disease, increased survival, and slight liver change. Another group of guinea pigs were exposed to a mixture of 13,000 ug/m³ SO₂ plus 500 ug/m³ of respirable particulate. No deleterious effects were observed. This finding pertains to the functional, as well as the morphologic parameters recorded. In this group of guinea pigs, the liver cells disclosed no

vacuolation as was observed in the animals not inhaling particulate material. We do not understand the significance of this difference. Vacuolation in rodent liver cells may signify reversible adaptive changes of little health consequence. That this minimal response was not recorded in the animals breathing SO_2 plus particulate can be taken as evidence that the combination exposure imposed no undue stress on the animals. A pair of experiments was conducted with guinea pigs exposed to sulfuric acid mist alone or combined with particulate.

TABLE I -- Effects on Guinea Pigs of Chronic Exposure to SO_2 and Particulate

<u>Nominal Concentrations</u>	<u>Results</u>
SO_2 13,000 $\mu\text{g}/\text{m}^3$	Increased Lung Diffusion Reduced Lung Disease Increased Survival Rate Liver Cell Vacuolation
SO_2 13,000 $\mu\text{g}/\text{m}^3$ with 500 $\mu\text{g}/\text{m}^3$ Particulate	Normal Lung Diffusion Normal Lung Disease Normal Survival Rate No Liver Cell Vacuolation

Tables II and III summarize the results. Significant harm to these animals occurred when the guinea pigs receiving 610 $\mu\text{g}/\text{m}^3$ (0.610 mg/m^3) were accidentally exposed to 2,300 mg/m^3 for about 20 minutes. As consequences of this event, one-third of the animals died, and respiratory dysfunction and lung injury occurred. Recovery in lung function was noted in three weeks after the over-exposure when the guinea pigs were exposed to filtered air only, not H_2SO_4 aerosol. Because the high level exposure in this experiment was aborted by the accidental over-exposure, an additional group was exposed to 900 $\mu\text{g}/\text{m}^3$. Only a reduction in growth rate was noted in this experiment, and this was not attributable to H_2SO_4 exposure because of the

absense of any respiratory or pulmonary changes usually associated with inhalation of an irritating aerosol.

TABLE II - Exposure of Guinea Pigs to H_2SO_4 Aerosol⁽¹⁾

H_2SO_4 Concentration ug/m ³	Particle Size microns	Results
-0-	-	No deleterious effects
80	<1	Reduced growth rate only
100	>1	Reduced growth rate only
610 ⁽²⁾	<1	30% mortality Reduced growth rate Increased respiratory resistance Lung injury (acute) Recovered in three weeks
900	<1	Reduced growth rate only

(1) Exposed 12 months, 22 hours daily.

(2) Accidental overexposure at week 23 to estimated concentration of 2,300 mg/m³, 20 minutes.

In the combination experiment (Table III) in which guinea pigs inhaled H_2SO_4 aerosol mixed with particulate at concentrations of 80 ug/m³ H_2SO_4 with 450 or 460 ug/m³ particulate, no deleterious effects were demonstrated functionally or anatomically. Not even was a reduction in growth rate observed which had been noted (Table IV) in guinea pigs exposed to 80 or 100 ug/m³ of H_2SO_4 aerosol. Reduction in growth rate would seem not to be critical in assessing effects of these inhaled toxicants whose primary point of attack is on the respiratory system at least without other evidence of systemic toxicity.

TABLE III - Exposure of Guinea Pigs to Particulate and H_2SO_4 Aerosol (1)

Combined Agents	Concentration ug/m^3	Particle Size microns	Results
H_2SO_4 + Particulate	80 460	<1 <5	No deleterious effects
H_2SO_4 + Particulate	80 450	1-5 <5	No deleterious effects

(1) exposed 12 months, 22 hours daily

Monkeys exposed continuously to 250, 1,250 or 2,500 ug/m^3 SO_2 for 18 months experienced no detrimental effects of these SO_2 levels (Table IV, Phase I). At 13,000 ug/m^3 , there were no changes attributable to exposures during the first 30 weeks. At this time, the animals were accidentally over-exposed to approximately 200 to 1,000 ppm (0.5×10^6 - 2.5×10^6 ug/m^3) with immediate reactions in pulmonary functions, increase in the alveolar macrophage population, and thickening of the bronchiolar and alveolar walls.

TABLE IV -- Results of SO_2 Overexposure of Monkeys

<u>Phase I</u>	<u>Exposure Sequence</u>	<u>Observations</u>
Weeks 1-30:	13,000 ug/m^3 SO_2	O.K.
Week 31:	200-1,000 ppm SO_2 x 60 minutes	Increased Respiratory Rate Impaired Lung Ventilation
Weeks 31-78:	Filtered Air No SO_2	Low Arterial O_2 Liver Cell Vacuolation Alveolar Macrophages Increased Thickening of Alveolar and Bronchiolar Walls
<u>Phase II</u>		
Weeks 1-78:	13,000 ug/m^3 SO_2	Increased Growth Rate Improved Lung Ventilation Normal Lung Histology

As shown in Table IV, Phase II, a continuous exposure at 13,000 ug/m³ for 78 weeks, without the intervention of an over-exposure, effects on health attributable to SO₂ were not observed.

Tables V and VI disclose no harmful effects on monkeys exposed for 18 months from these concentrations of respirable particulate at 500 ug/m³ alone or in combination with SO₂ at levels of 250, 2,500 or 13,000 ug/m³.

TABLE V -- Exposure of Monkeys to Particulate

<u>Concentration</u>	<u>Particle Size Average</u>	<u>Exposure Duration</u>	<u>Observations</u> (1)
160 ug/m ³	5u	18 months	No harmful effects
460 ug/m ³	5u	18 months	No harmful effects

(1) Included: Body weight, survival, clinical chemistry, behavior, respiratory functions, pathology

TABLE VI -- Effects of Exposure of Monkeys to SO₂ and Particulate Combinations (18 Months)

<u>Nominal Concentrations</u>			<u>Results</u>
<u>SO₂</u> <u>ug/m³</u>	<u>Particulate</u> <u>ug/m³</u>	<u>Particle</u> <u>Diameter</u> <u>u</u>	
250	500	< 5	Increased growth
2,500	500	< 5	No deleterious effects
13,000	500	< 5	on lung function, blood and biochemical parameters or histology

When monkeys were exposed continuously for 18 months, as shown in Table VII to sulfuric acid aerosol at levels of 380 ug/m³ to 4,790 ug/m³ employing two particle size ranges, two deaths occurred from pulmonary hemorrhage, and significant functional changes occurred.

TABLE VII -- Effects on Monkeys of Inhaling H₂SO₄ Aerosol (18 months)

Concentration ug/m ³	Particle Diameter	Effects*
2,430	1-5u	1, 2, 3, 4
380	1-5u	1, 4 (slight)
4,790	1u	1, 2, 3, 4
480	1u	2 (slight)

- * 1. Increased Respiratory Rate
- 2. Impaired Lung Ventilation
- 3. Lowered Arterial Oxygen
- 4. Lung-Epithelial Hyperplasia, Thickening of Bronchiolar Wall

Evidence of functional changes included increased respiratory rate, deterioration in the distribution of inspired air, and lowered arterial oxygen content. The two lower concentrations were associated with lesser effects. Diffusional capacity of the lung was not affected at any concentration. Alteration of the lung structure included epithelial hyperplasia and thickening of the bronchiolar wall.

When combined with particulate at 500 ug/m³ (<5 u diam), a sulfuric acid aerosol concentration of 990 ug/m³ produced structural changes in the lungs of monkeys that were similar to those observed when particulate was not present in the atmosphere. No such alterations were observed at the lower sulfuric acid aerosol concentration of 110 ug/m³ combined with a particulate concentration of 500 ug/m³.

It is evident that the particulate present in these chambers exerted little if any influence on the response to inhaled sulfur dioxide or sulfuric acid aerosol. The latter proved to be the greater irritant to the respiratory system.

Exposures of monkeys 22 hours a day for 2 years to 10,000 ug/m³ calcium sulfate produced no functional or anatomic abnormality. Observations or measurements included: body weight, hematology, blood gases, respiratory functions, clinical biochemistry, organ weight, and pathology. Even when 25,000 ug/m³ of sulfur dioxide were mixed with 10,000 ug/m³ of calcium sulfate, no detrimental changes were observed in the same parameters cited above.

These toxicologic investigations bear on potential human health effects in several ways.

1. Except at concentrations exceeding 13,000 ug/m³, i.e., overtly irritating sulfur dioxide per se does not appear to be an air pollutant of concern to a healthy population. Even when mixed with respirable particulate collected from fossil fuel-burning electric generating plants, sulfur dioxide was not harmful to guinea pigs or monkeys. This particulate was relatively insoluble, and little conversion to sulfate is suspected.
2. The oxidation products of sulfur dioxide are of concern, even to a healthy population particularly sulfuric acid aerosol, as judged by these experiments using guinea pigs and monkeys.
3. We know that differential susceptibility to air pollutants in the human population inveighs against uniformity of response. By using different animal species, and approximation to the human situation is feasible and dose-response data can be obtained - a feature not readily obtainable from epidemiology.
4. This toxicologic study has clearly revealed that all sulfate compounds do not act alike as pulmonary irritants. For example, we have shown that calcium sulfate is several orders of magnitude less a toxic irritant than sulfuric acid aerosol. This finding aptly demonstrates that animal experiments can sort out the more

hazardous substances from those which are less so. On the basis of relative toxicity as derived from animal investigations, priorities can be defined for controlling certain pollutants and criteria can be developed for assessment of health effects.

Of course toxicological data are inferential in nature. Animal experiments yield inferential data in that animal species may differ markedly among themselves and also may be quite different from man in reacting to foreign substances. Man may be more or less susceptible than any one animal species, and it is not possible to decide a priori which animal species is closest to man. Further, the homogeneity of animal groups does not at all copy the variegated human population at risk. And, finally, the stresses of human society are usually not part of a well controlled animal study. The stresses experienced by man may make him more or less susceptible to attack from pollutants.

Even data derived from human experiments are inferential because of the small numbers of experimental subjects relative to the vast number of their brothers, the relative brevity of the experimental exposure relative to the duration of most hazards, and the variety of physiological conditions and psychological stresses resident in modern human society that cannot be adequately incorporated into a human experiment.

The decision to establish an environmental standard with a finite probability of human exposure involves balancing the toxicological risks of use against the benefits of use in society. Many factors bear on this decision. Animal studies provide a preliminary or initial basis for the judgment. Acute and chronic toxicity studies are fundamental in establishing safety guidelines for the hazards involved in the use of a substance. Functional and mechanism studies should assume a greater role in the decision. There is a need for experimental designs to be closely related to use patterns to enhance the validity of the inferences from toxicological data. Ultimately, the decision leading to an environmental standard is a judgement,

reflecting some personal or social system of values, and it is based on experience in actual use and documented by continuing epidemiologic studies of the populations at risk.

DISCUSSION

GOLDSMITH (U.S.A.)

Your data appear to show that there is impairment of growth rate by levels of H_2SO_4 as low as $80 \mu g/m^3$ in guinea pigs, with particle size $\leq 1 \mu g$. How should such effects be interpreted with respect to human health?

CLAYTON (U.S.A.)

Such effects should be interpreted with caution. Unless body weight changes are accompanied by other, related dysfunctions they should not be anticipated as significant to human health effects.

LAFONTAINE (Belgium)

My question is perhaps more of a comment than an actual question: experimental exposure to SO_2 , H_2SO_4 aerosols, and certain combinations of SO_2 and particulates should be accompanied by exposures to bacteria or viruses with varying degrees of pathogenicity. This would permit closer comparison with the effects in humans and would perhaps explain the scatter found in the results. We must, of course, consider measurements made in the atmosphere (SO_2 and particulates) as nothing more than indices.

CLAYTON (U.S.A.)

I agree with Dr. Lafontaines' comment. Studies on this issue show that intercurrent infection with microorganisms is exacerbated by inhaled irritants.

NEWHOUSE (Canada)

I question the validity of the animal model and the axiom that toxicologic data can be extrapolated in large part to man. I base my comments on the alterations noted by Proctor in nasal mucociliary transport in normal man exposed, to 5 or even 1 ppm SO₂, alone during short-term acute exposures, as well as data from our laboratory (and others) showing significant changes in the maximum midexpiratory flow rate (an index of probably small airway obstruction) during similar exposures. While this may not have important implications in chronic exposure conditions it does, I believe, cast some doubt on the validity of the animal model.

CLAYTON (U.S.A.)

As I made clear in my statements in this paper, extension to man should be made with conservatism. Your data appear interesting but a dose-response curve should be obtained at levels <1 ppm in order to increase the relevance for ambient conditions.

BIOLOGICAL EFFECTS OF THE POLYCHLORINATED BIPHENYLS IN NONHUMAN PRIMATES

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ABSTRACT

Daily ingestion of polychlorinated biphenyls (PCBs) at doses between 25 ppm and 300 ppm over a period of 2 to 3 months caused morbidity and mortality in nonhuman primates (*Macaca mulatta*). Changes included loss of body weight, alopecia, subcutaneous edema, acne, conjunctivitis, ascites, hydrothorax, gastric mucosal hyperplasia, liver hypertrophy and bone marrow hypoplasia. Terminally, these animals had decreased hemoglobins, hematocrits and serum protein, shifts in the serum albumin to globulin ratios and a neutrophilia. A dose of 2.5 ppm PCB in the diet was sufficient to cause alopecia, focal edema and conjunctivitis in monkeys within 2 months. Animals that have survived the ingestion of 250 to 300 mg of PCB over 2 months maintained levels of PCB in their adipose tissue for periods in excess of 1 year. In addition, offspring of these animals had detectable levels of PCBs in their tissues.

In contrast to the injurious effects experienced by adult nonhuman primates exposed to PCBs, one-month-old infant monkeys that were exposed to 1g of PCB for 30 days were essentially free of any of the clinical, gross and microscopic alterations of PCB intoxication. These observations as well as metabolic studies suggest that the metabolism of the PCBs is important in determining their toxicity.

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1. Introduction

Although the polychlorinated biphenyls (PCBs) have been used extensively for industrial purposes for over 40 years, it has only been during the last decade that they have been regarded as environmental contaminants (Jensen [1]). These compounds are extremely stable, not hydrolyzed by water, acids or alkali, and are able to withstand temperatures up to 650°F without disintegrating. They have been used in elastomers adhesives, paints, varnishes, printing inks, putty, and as general fillers. Since they do not conduct electricity, they have also found widespread use in electrical equipment such as transformers. Their stability and low vapor pressures make them well suited as lubricants, hydraulic fluids, liquid seals, cutting oils, vacuum diffusion pump oils, and as vapor suppressants and insecticide formulations. The same properties that make them ideal for commercial use also enhance their resistance to degradation in the environment. The magnitude of PCB contamination is further exemplified by their presence in coho salmon, milk fat, poultry, eggs, and fish (Kolbye [2]). Primarily as a result of food contamination, detectable levels of PCBs were found to be present in over 30% of randomly sampled inhabitants of the United States (Yobs [3]).

Early outbreaks of PCB intoxication were limited to industrial accidents where workers reported incidents of chloracne (Jones and Alden, [4], Good and Pensky [5]). It was not until 1968 that the greater health significance of PCB exposure became known. Following the consumption of PCB contaminated rice oil by over 1,000 Japanese, diverse symptoms and lesions developed. These persons became nauseated and lethargic, and developed chloracne and subcutaneous edema. Infants born to exposed mothers were small and exhibited discolored skin and had an abnormal eye discharge. Many of the symptoms and lesions that developed during the acute phase of the illness have persisted for years (Kuratsune [6], Kuratsune et al. [7]).

2. Experimental Studies

2.1 High Level PCB Exposure. In order to further clarify the biological effects of various levels of PCB exposure in primates, a series of experiments have been conducted. In these experiments, adult Macaca mulatta monkeys were given diets containing 25, 100, and 300 ppm of a PCB (Aroclor 1248, Monsanto Co., Inc., St. Louis, Missouri, U.S.A.) for periods of 2 to 3 months (Allen and Norback [8], Allen et al. [9],

[10]). Although each of these dosages produced signs and lesions compatible with PCB intoxication within one month, the total PCB intake varied from 250 to 400 mg for the 25 ppm group, 0.8 to 1.0 g for the 100 ppm group, and 3.6 to 5.4 g for the 300 ppm group. Mortality occurred in the groups receiving the two larger doses within 2 months and within 4 months on the lower regime. Hematological changes developed gradually during the period of experimentation; however, they were most obvious in the 300 ppm group. These animals showed a decrease in hemoglobin (grams per 100 ml) from 13.0 ± 1.0 to 10.6 ± 0.3 within 12 weeks, and a corresponding decrease in hematocrit from $39.0 \pm 2.0\%$ to $32.0 \pm 1.0\%$. Although the total white cell count was not appreciably altered, there was a decrease in the number of lymphocytes and a concomitant increase in the neutrophil population. Decreases in the level of serum protein were accompanied by a reduction in the percentage of albumin and increases in the globulin fraction. Reduced levels of serum lipids, cholesterol, and triglycerides accompanied the alterations in serum protein (Allen *et al.* [10]).

A gradual weight loss was recorded throughout the experimental period for all PCB-fed animals. The 25% decrease in body weight of the 300 ppm group was particularly striking. Following one month of exposure, there was moderate to marked loss of hair from the head, neck, and back, and edema of the mouth and eyelids. Loss of eyelashes, excessive lacrimation, and conjunctival congestion were also apparent. Small pustules involving hair follicles were particularly obvious around the mouth and on the cheeks and neck.

Liver biopsies taken from the animals after a short period of exposure to PCBs showed a decided increase in the smooth endoplasmic reticulum of the hepatic cells (Figure 1). Biochemically, the liver homogenates contained decreased levels of DNA (mg/mg liver) and RNA (mg/mg DNA) and increased levels of protein (mg/mg DNA) and increased activity of microsomal mixed function oxidases. In those animals that were sacrificed, the enlarged livers continued to show proliferation of the endoplasmic reticulum. However, instead of the endoplasmic reticulum being distributed throughout the cytoplasm it was arranged in distinct packets of closely associated membranes (Figure 2). Microsomes prepared from those livers showed a decided decrease in activity of mixed function oxidases (Allen *et al.* [9]).



FIGURE 1. Hepatocytes obtained from a liver biopsy of a monkey that had received 300 ppm PCB in the diet for 2 weeks. Note the abundant smooth endoplasmic reticulum (SER) and short segments of rough endoplasmic reticulum (RER). Normal appearing mitochondria (M) are randomly dispersed among the ER. Small lipid droplets (L) appear as round lucent areas in the cytoplasm. X 8,420.

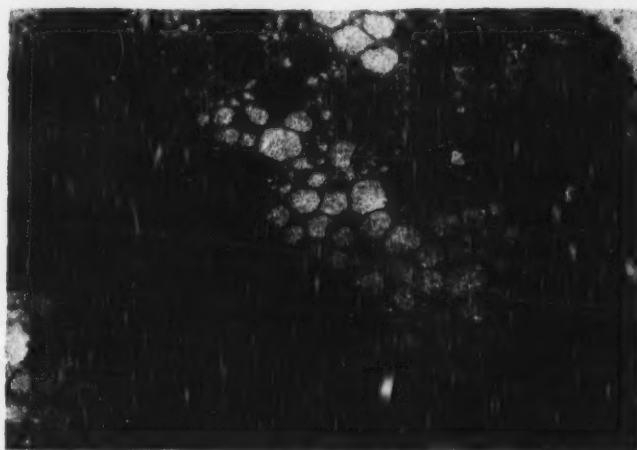


FIGURE 2. Large dense packets of smooth endoplasmic reticulum (SER) prevail in the cytoplasm of hepatocytes obtained from monkey exposed to 300 ppm PCB in the diet for 2 months. Microsomes prepared from liver cells having similar morphological features were hypoactive enzymatically. Abundant lipid droplets prevail in the cytoplasm not occupied by ER. The mitochondria (M) appear normal. X 6,920.

The most severe pathological changes recorded at necropsy were located in the stomach where marked hypertrophy of the mucosal lining and edema of the stomach wall, particularly of the fundic and pyloric regions, were apparent. Microscopically, the hypertrophic, gastric mucosa was several times thicker than the control mucosa and was comprised of greatly elongated hyperplastic glands containing mucous secreting cells (Figures 3 and 4). Prevention of discharges of the secretions owing to the depth and apposition of the glands predisposed to the development of large mucous cysts. There was also widespread penetration of the muscularis mucosae with invasion of the submucosa by the mucosal epithelium. There were microscopic lesions of the skin, particularly of the face, of PCB-exposed animals. Numerous intrafollicular cysts surrounded by edematous, leukocyte-filled connective tissue were apparent.

At necropsy a portion of the tissues from the animals was obtained for the determination of PCB levels by the previously reported gas chromatographic procedures (Allen *et al.*, [9]). Sites of major storage, in addition to fat, were the adrenals, liver, and pancreas.

The persistence of the PCBs in the tissues of exposed animals was demonstrated in the group receiving 25 ppm PCBs in the diet for 2 months (total intake approximately 300 mg). Immediately after the PCB-supplemented diet was discontinued, the subcutaneous adipose tissue contained an average of 127 μg per g fat (Allen *et al.* [11]). Even after one year, concentrations of PCBs in the fatty tissue averaged 30 μg per g fat. Additional distribution data were obtained from a PCB-fed female that delivered an infant eight months after being taken off the PCB diet. Levels of PCB ($\mu\text{g/g}$ tissue) in the adipose tissue of this infant were approximately one-half that present in the tissues of the mother, thus indicating transplacental movement of these compounds (Allen *et al.*, [11]).

2.2 Low Level PCB Exposure. Recently, experiments have been initiated to determine if levels of PCBs permitted in foods destined for human consumption would be toxic when consumed on a continuous basis. Adult rhesus monkeys are being given diets containing 2.5 and 5.0 ppm PCBs (Aroclor 1248). These levels are one-half and equal to the levels permitted in certain foods. Interestingly enough, these animals developed loss of hair and eyelashes within 2 to 3 months. They also have swollen upper eyelids and congested conjunctiva.



FIGURE 3. The gastric mucosa of a normal adult rhesus monkey is depicted. Note the narrow band of muscularis mucosae(M) and underlying submucosa (SM) and smooth muscle (S) components of the stomach wall; hematoxylin and eosin stain. X 25.



FIGURE 4. Stomach of a monkey that had received 300 ppm PCB in the diet for 2 months. Note the hyperplastic gastric mucosa and presence of dilated glands. The majority of the submucosa has been replaced by glandular elements of the mucosal epithelium. Note the large cystic spaces that have resulted from the stasis of mucous in these glands (C); hematoxylin and eosin stain. X 25.

2.3 Infant Studies. In order to determine if adult and infant primates would respond similarly to PCB exposure, one-month-old rhesus monkeys were given 1 g (35 mg/kg body weight) of PCB over a 30 day period. The total consumption of PCBs by these infants was essentially the same as that received by the adults given 100 ppm in the diet as mentioned previously. These animals were able to survive without any obvious ill effects at doses that had been fatal to adults (Abrahamson and Allen, [12]). When the tissues from the infant and adult monkeys were evaluated chromatographically it was established that the concentration of PCB was lower and fewer isomers were present in the adult tissues. Those isomers that were present in infants and absent in the adult tissues consisted primarily of those having lower chlorine levels (Table 1).

TABLE 1. CHROMATOGRAPHIC DATA ON ADIPOSE TISSUE OBTAINED FROM RHESUS MONKEYS EXPOSED TO AROCLOR 1248^a

Retention Time (Sec)	Standard	Mother ^b	Newborn Infant ^c	Adult ^d	Infant ^e
57	0.12	7.70		1.56	0.17
73	2.85				
82	4.07				14.04
102	18.45				
130	6.91				14.27
146	1.52	2.80			
156	1.30				
201	40.12	10.49		19.33	47.56
236	2.86	7.58			7.93
306	10.61	0.30	11.34	63.52	11.63
392	7.65	50.96	4.14	15.57	3.92
472	3.46	20.14	76.79		0.47
507	0.03		7.17		

^a Monsanto Co. Inc., St. Louis, Missouri U.S.A.

^b Tissue taken from female monkey at time of cesarian section, 8 months after discontinuation of PCB diet (total PCB intake - 300 g).

^c Infant tissue taken immediately following cesarian delivery.

^d Tissues of adult monkey taken after 1 month on PCB diet (total PCB intake - 1 g).

^e Tissue from infant monkey taken after 1 month on PCB diet (total PCB intake - 1 g).

2.4 Metabolic Studies. Metabolic studies were conducted in adult rhesus monkeys that had been given a single intragastric dose of a PCB containing multiple isomers (Aroclor 1248) and a single isomer (2,5,2',5'-tetrachlorobiphenyl). It was demonstrated that approximately 90% of the compound was absorbed from the gastrointestinal tract. Ten percent of the original dose was detected chromatographically in the urine and feces within 14 days with the greatest percentage being excreted between the second and eighth day. When similar studies were conducted with tritiated 2,5,2',5'-tetrachlorobiphenyl, approximately 85% of the radioactivity was recovered, primarily in the feces within 2 weeks, and majority of it was eliminated by 72 hours. An additional 10% was detected in the animal tissues. Of the PCB that remained in the animal, the largest percentage was present in the adipose tissue and secondly in organs having high fat content.

3. Discussion

When nonhuman primates were exposed to levels of PCBs similar to that experienced by the Japanese in the 1968 PCB outbreak, they developed signs and lesions similar to those recorded in human cases. Subcutaneous edema, particularly around the eyes and lips, and hyperemic conjunctivitis with excessive secretion of the Meibomian glands were consistently present. There were also follicular accentuations of the skin characterized by dilatation of the sebaceous ducts and development of keratin cysts. The severely affected patients and primates had a decrease in erythrocytes, reduced hemoglobin, and a neutrophilia. Although not documented in the exposed humans, the nausea and anorexia they experienced was suggestive of a gastritis as was the case in the experimental animals. Liver hypertrophy, proliferation of the hepatic endoplasmic reticulum, and increased microsomal enzyme activity were apparent in both species. In addition, the persistence of these lesions for extended periods following the discontinuation of PCB exposure was recorded in the Japanese outbreak and has also been observed in experimentally exposed nonhuman primates.

The data and observations cited in this report clearly indicate that PCBs are toxic to primates over a wide dose range. Particularly significant is the appearance of lesions within less than 2 months in monkeys that were fed diets containing 2.5 and 5.0 ppm. Although the intake of PCBs by these animals was on a continuous basis and the likelihood of the

general population consuming a diet containing this quantity of PCBs is small, it does point out that only small amounts of these compounds are required to produce toxicity in primates. In addition, since PCBs accumulate in tissues of exposed mammals, continuous exposure to even very minute amounts may eventually reach a level sufficient to cause toxic manifestations.

It is of interest that the toxicity of PCBs in infant and adult monkeys is markedly different. Levels of exposure that were fatal to adults produced no gross effects in one-month-old infants. It has been shown that infant monkeys have a poorly developed mixed function oxidase system (Allen and Chesney [13]). These observations are further substantiated by the chromatographic data obtained on the tissues of the two age groups of animals. Adult tissues contained lower levels and fewer isomers of PCBs than did the infant tissues, thus indicating more rapid metabolism or excretion of these compounds by older animals. These data suggest that PCB metabolites are responsible for the deleterious effects produced by PCBs in monkeys.

Unlike primates, infants of lower animals suffered much more severely from PCB exposure than did adults (McLaughlin *et al.* [14], Keplinger *et al.* [15], Dahlstrom [16], Hays and Risebrough [17], Ringer *et al.* [18], DeLong *et al.* [19]). Clarification of these findings was recently obtained in rats by the use of liver enzyme inhibitors (SKF 525-A -- p-dimethylaminoethyldiphenylpropylactate and chloramphenicol) and inducers (phenobarbital). In these experiments, rats pretreated with enzyme inhibitors, which may parallel the enzymatic status of the infant liver, experienced heavy mortality while animals pretreated with enzyme inducers suffered no deaths. Thus it would appear that the metabolism of PCBs may be necessary for toxicity in monkeys while the reverse may be true in rats.

Many of the lesions that develop in PCB intoxicated primates may be directly related to tissue exposure to the PCBs while other lesions may be secondary. The loss of weight, decrease in serum protein and moderate anemia could be related to the reduced food intake that occurs in the animals with severe hyperplastic gastritis which develops as a result of the irritating effects of the PCBs on the gastric mucosa. The hypertrophic hyperactive livers that develop in these animals are a result of the stimulatory effects of these compounds on the hepatic endoplasmic reticulum. However, when the liver exposure to the PCBs is sufficiently

great, degenerative changes develop particularly in the organelle containing the majority of PCBs, the endoplasmic reticulum. The skin lesions may also be directly related to localization of high levels of PCBs in their tissue. Keratinization of the sebaceous gland ducts and hair follicles following the irritating exposure to PCBs leads to formation of keratin cysts. In addition, edema and inflammation that develops around the effected glands and hair follicles may be a direct result of injurious effects on these tissues by the PCBs.

Many of the lesions that develop following PCB exposure may result secondarily from the increased metabolism of endogenous substances by the hyperactive hepatic endoplasmic reticulum. Following PCB exposure there is enhanced metabolism of steroid and steroid-like compounds. Vitamin A which is steroid-like compositionally is deficient in quail, rats (Bitman et al. [20]) and monkeys (Allen, unpublished observations) following PCB exposure. Since vitamin A deficiencies resulting from an increased rate of metabolic decomposition have been reported to produce gastric hyperplasia (Cramer [21]), gastric carcinoma (Fujimaki [22]), and follicular dermatitis (Mason [23]), it is not unlikely that a deficiency of this vitamin may be responsible at least in part for many of the lesions resulting from PCB intoxication.

Acknowledgements

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DISCUSSION

WASSERMAN (Israel)

It would be of high epidemiological interest to learn about the following biological effects observed in the Japanese population poisoned by PCB's.

Among the biological effects produced by PCB's, the decrease of PBI and the hyperactivity in the hypophyso-thyroidadrenal axis was observed by us. Tribute should be paid to Jensen for detecting the PCB's in man, a finding which opens a new view in man's exposure to environmental hazards.

ALLEN (U.S.A.)

The residual effects of polychlorinated biphenyl intoxication in man seem to be long lasting. According to Dr. Kuratsune of the Department of Public Health, Kyushu University in Japan, many of those persons who were exposed to the PCB contaminated rice oil continue to show ill effects after 3 years. We would suggest that Dr. Kuratsune be contacted about the levels of PBI and hyperactivity in these patients as related to the hypophyso-thyroid adrenal axis. Furthermore, it goes without saying that all of us are indebted to Dr. Jensen and his astute observations which exposed the PCB problem.

CLAUDE (France)

In your text you mention the reduced blood level of cholesterol and triglycerides after intake of PCB. One could make the hypothesis that there was a blockage of hepatic secretion of the lipoproteins. Have you made chemical or histological observations showing a certain frequency of hepatic steatosis which would confirm the above hypothesis?

ALLEN (U.S.A.)

These animals do have a moderately fatty liver. However, we have no data that would indicate one way or the other if this fatty liver is related to the blockage of lipoprotein secretion by the liver. In addition, we are not aware of any other data along these lines from other laboratories.

CHAMBERS (Ireland)

I note that Dr. Allen did not make any reference to the immuno-suppressive effect of the PCBs which has been described in other animals, rabbits I believe, by workers in Utrecht. Is this phenomenon not considered to occur in monkeys?

ALLEN (U.S.A.)

Experiments along these lines on monkeys have not been conducted. It can be said, however, that these animals do become leukopenic and are much more susceptible to opportune pathogens. Whether this is related solely to their debilitated condition or to an immunosuppressive effect of the PCBs is not clear.

UNTERSUCHUNG DER WIRKUNGEN AUF DEN MENSCHEN
EXPOSURE MONITORING
MESURE DE L'EXPOSITION
MISURA DELL'ESPOSIZIONE
METING VAN EXPOSIE

Panel

Vorsitzender - Chairman - Président - Presidente - Voorzitter

M.J. SYROTA (France)

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RECAPITULATION OF ENVIRONMENTAL EXPOSURES

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ABSTRACT

In order to quantitate the effects of air pollutant exposure on diseases such as chronic respiratory disease, annual estimates of air pollutant concentrations for approximately twenty years are required. This paper describes general techniques for the recapitulation of environmental exposure under a wide variety of topographic, climatic and source emission distribution conditions. Annual wind rose and atmospheric stability conditions are analytically coupled with source emission data to estimate past spatial distributions of various pollutants.

Example recapitulations of sulfur dioxide concentrations and total suspended particulate concentrations are presented for both densely populated areas such as Metropolitan New York, and sparsely populated areas such as Helena, Montana. The use of dustfall data as an indicator of other pollutants such as suspended sulfates is examined statistically. Methods are described for calibrating computer based air pollution meteorological models to local topographic and climatic conditions. Techniques for determining the limits of precision of air pollutant exposure estimates are described.

Measurements of air pollutant exposure for communities in the vicinity of Los Angeles constitute a data base upon which estimates of air pollution concentrations for a 10,000 square mile area (the California South Coast Air Basin) are made.

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Annual average isoplethes for Oxidant, NO_2 and total suspended particulate are constructed for the time period from 1955 to 1972. Annual average isoplethes of the daily maximum hourly average concentrations which provide an estimate of the magnitude of peak air pollutant exposures are discussed and spatial distribution of Oxidant is presented. Long-term trends for 4 communities are described.

1. INTRODUCTION

Air pollution monitoring is a young science. Consequently, the methodologies used to measure pollutants change frequently. Furthermore, the number of sites at which the air is measured is rapidly increasing. This state of flux makes it difficult to recapitulate air pollutant historical exposures. In some locations which are very interesting from an epidemiological point of view, past exposure data may be very sparse. In other cases, the available air monitoring data may not be for a community near the city under investigation. In large cities such as New York there are gaps in the historical air quality records.

This paper presents techniques that have been used to estimate the values of past air quality under a wide variety of conditions. Various techniques are described for interpolation and extrapolation of available air pollutant measurements. These techniques include use of air quality models, construction of isoplethes from air monitoring station data and estimation of the value of one pollutant from measured values of another pollutant.

2. AIR QUALITY MODELS

Air quality models vary in sophistication from the simple "box model"[1] to very complex models which numerically estimate the space and time distribution of a pollutant through a set of coupled nonlinear differential equations[2]. The class of air quality simulation models[3] is intermediate in complexity. These models primarily use wind-stability roses coupled with gaussian diffusion of pollutants from sources of pollution to estimate ground level exposure. The relative merits of models is currently the subject of considerable debate.[4] The general precision, accuracy and applicability of a variety of models to air quality criteria pollutants will be carefully established in a Regional Air Pollution Study which is being conducted by the Environmental Protection Agency.

The goal of most all air quality models is to relate emissions to ground level exposure. In this paper various approaches are used to estimate exposures for a wide variety of locales ranging from smelter communities in the Rocky Mountains to large metropolitan cities such as Los Angeles and New York.

3. RECAPITULATIONS BASED ON PRODUCTION

Western smelting communities usually have little pollution from automobiles or from non-smelting industrial sources. Ambient air pollution in these communities is characterized by levels of both sulfur dioxide and total suspended particulates in excess of national primary air quality standards. Since smelters represent an approximate point source of pollutants, estimates of previous community exposures to both sulfur dioxide and particulates can be made through the use of production data.

Estimates of long-term exposure to sulfur dioxide, total suspended particulates, and suspended sulfates in the three smelter communities were based upon annual metal production data, estimates of stack emissions of both particulates and sulfur dioxide, and observed air quality measurements. Annual metal production estimates for each smelter^[5] were supplemented with actual production data and sulfur dioxide and particulate emissions data provided to the U. S. Environmental Protection Agency by each corporation.

Sulfur dioxide and particulate emission factors for copper smelting, lead smelting, and zinc smelting^[6] were applied to the annual metal production figures in order to determine average daily stack emissions of both sulfur dioxide and particulates.

By comparing observed air quality data to average daily pollutant emissions from a given isolated point source, one can estimate the ratio of annual average pollutant concentration to the average rate of pollutant emission from the point source. In the case of East Helena, annual average total suspended particulate concentrations

are available for the years 1966, 1967, 1968, and 1969. The average ratio of observed annual average total suspended particulate concentration to average daily particulate emitted is $1.05 \frac{\mu\text{g}/\text{m}^3}{\text{ton}/\text{day}}$. The range of the data is 0.50. Using the techniques of inefficient statistics described in Dixon and Massey,[7] the standard deviation of the data is estimated to be 0.24. Using the common scientific convention of expressing variation at the 50% confidence level, the ratio of TSP concentration to tons of particulate emitted per day is estimated to be $1.05 \pm .16 \frac{\mu\text{g}/\text{m}^3}{\text{ton}/\text{day}}$.

4. RECAPITULATIONS BASED ON ISOPLETHES

Measurements of air pollutant exposure for communities in the vicinity of Los Angeles is available from over forty separate locations extending back in time as far as 1955. Unfortunately, all stations are not available for every year. For example, in 1955 data from only seven stations is available; in contrast, data from thirty-four stations is available in 1972. Continuous monitoring instruments were used to record Oxidant, Nitrogen Dioxide and Sulfur Dioxide. Estimates of environmental exposures for communities where the air was not monitored can be made by constructing a set of isoplethes for each pollutant for each year. The pollutant values for the communities of interest can then be read directly from the isopleth maps. The isoplethes are constructed by linearly interpolating the values observed at pairs of adjacent stations on a line connecting the stations. This process is repeated for all adjacent site locations except those where topographic considerations, such as a mountain, would invalidate the interpolation. Pollutant concentrations at nearby locations external to the network of stations can be estimated through linear extrapolation. Smooth lines are drawn between locations of equal pollutant concentration. In cases where doubt or ambiguity exists, concerning the detailed shape of a segment of the isopleth, more detailed interpolations can be made to resolve the problem. Historical trends are obtained by estimating the annual exposures at the communities of interest from the isoplethes and graphically showing these values as a function of year. Examples of oxidant

trends for several Los Angeles communities are shown in Figure 1.

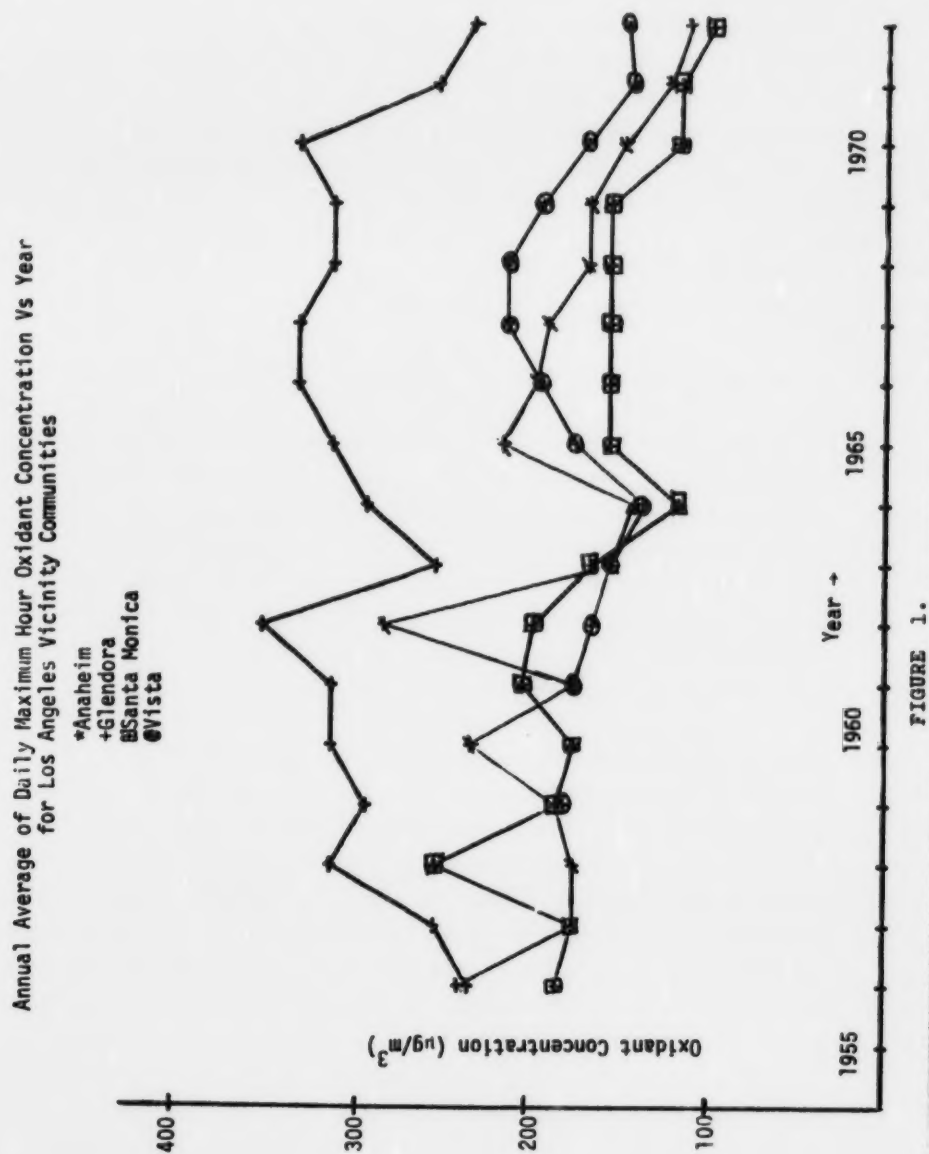


FIGURE 1.

5. RECAPITULATIONS BASED ON INDICATORS

Indicators of pollution such as dustfall readings can be used to estimate values of other pollutants such as sulfur dioxide or suspended sulfates. Examinations of New York City data over the time period 1954 through 1970 indicated that the ratio of the annual average of suspended sulfate to the annual average of dustfall did not appear to change substantially with year. The data indicated that this ratio was $11.5 \pm 1.5 \frac{\mu\text{g}/\text{m}^3}{\text{g}/\text{m}^2\text{Mo}}$. This ratio was used to estimate the values of suspended sulfate for years where dustfall data existed and suspended sulfate data did not. The above approach could not be used for sulfur dioxide estimates, since the available data indicated that the ratio of annual average of SO_2 to the annual average of dustfall did show a significant time trend.

6. CONCLUSIONS

Methods for recapitulation of past environmental exposures based on production data, isoplethes and pollution indicators have been described. Estimates of the accuracy of these techniques have been provided. These approaches provide a useful method of estimating past exposures to air pollutants.

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SAMPLING, ANALYSIS AND COMPOSITION OF AIRBORNE PARTICULATE MATERIAL IN BELGIUM

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ABSTRACT

During one year, aerosols have been sampled at 14 industrial, urban and rural locations in Belgium. At each station daily 24 hour samples were taken on cellulose filters. All samples were analysed for total suspended particulate and a large number for about 40 inorganic components including most metals and halogens. When properly summed, the measured constituents account for 50 to 75% of the total aerosol mass. The analytical techniques applied include instrumental neutron activation analysis, flameless atomic absorption and gravimetry.

Mean, maximum and most frequent values at all 14 stations for total suspended particulate and typical chemical compositions were calculated. The variation of the levels over the country and under the influence of the meteorological parameters are discussed. The generally much higher ambient air levels in industrial and urban areas, than in rural areas, give first indications for the pollution origin of the aerosols sampled. Inspection of the aerosol composition and its geographical distribution as a function of wind direction clearly indicate the existence of important localised emission sources for elements such as iron, zinc, cadmium, selenium, antimony, indium, silver, mercury, etc.

Intensive area-wide simultaneous samplings in industrial and urban areas reveal the existence of strong concentration gradients in the neighbourhood of steel plants and non-ferrous industries. Measurements of the mass versus aerodynamic particle size for all elements, by means of 8 stage cascade impactors, give information on the penetration and retention in the lungs.

1. Introduction

A 14 station aerosol sampling network was set up in order to evaluate the particulate levels in the ambient air over Belgium. During the period of October 1972 to October 1973 daily 24 hour samples were taken at all 14 stations. The sampling locations included the 5 major residential centra of Belgium namely Gent, Antwerpen, Brussel, Liège, Charleroi (GR, AR, BR, LR, CH) and the adjoining industrial areas (GI, AI, LI). Samples were also taken in the medium-sized city Mechelen (ME), in the rural areas of Ploegsteert and Mol (PL, ML), in the background stations Houffalize and Dourbes (HF, DB) and in a sea-coast station Zeebrugge (ZB).

The samplers used in this study have been described extensively by Dams and Heindryckx [1]. They consist of a high vacuum rotary pump equipped with a flow- and vacuum-meter and a 10 cm diameter P. V. C. filterholder placed in a protective P. V. C. shelter. On these samplers Whatman 41 cellulose filters are being used at a flow rate of approximately 400 m^3 per 24 hours which results in the collection of 10 to 100 mg particulate material.

A number of days with relatively constant wind directions was selected for chemical analysis of 35 elements in the particulate material. These selected samples were analysed by instrumental neutron activation analysis using a simplified irradiation-counting scheme (Dams et al. [2], Heindryckx and Dams [3]). A short neutron irradiation was followed by a 8 min gammaspectrometric count on a Ge(Li) detector after a decay period of 6 min. After a longer irradiation, cooling times of 1 to 3 days and 15 to 20 days were allowed for two additional gamma-spectrometric measurements. The gammaspectra were recorded on magnetic tape and the data were automatically reduced with a PDP 9 computer. A limited number of the selected samples was analysed for some additional components. Sulphate, nitrate and ammonium were determined spectrophotometrically. Silicon was measured after activation with 14 MeV neutrons and fluorine by reactor neutron activation using a very short irradiation and counting scheme, owing to the small half-life (11.2 s) of the isotope formed (Van Grieken and Dams [4], Dams et al. [5]). Cadmium and lead were determined by flameless atomic absorption (Janssens and Dams [6], [7]).

2. Total Suspended Particulate Matter (TSP)

Total suspended particulate matter is one of the basic components to be measured in air pollution studies and can be regarded as a good measure for general air quality. For all 14 Belgian stations mean levels, coefficients of variation and integrated frequency distributions have been calculated, the 50% and 95% levels are shown on a map in figure 1.

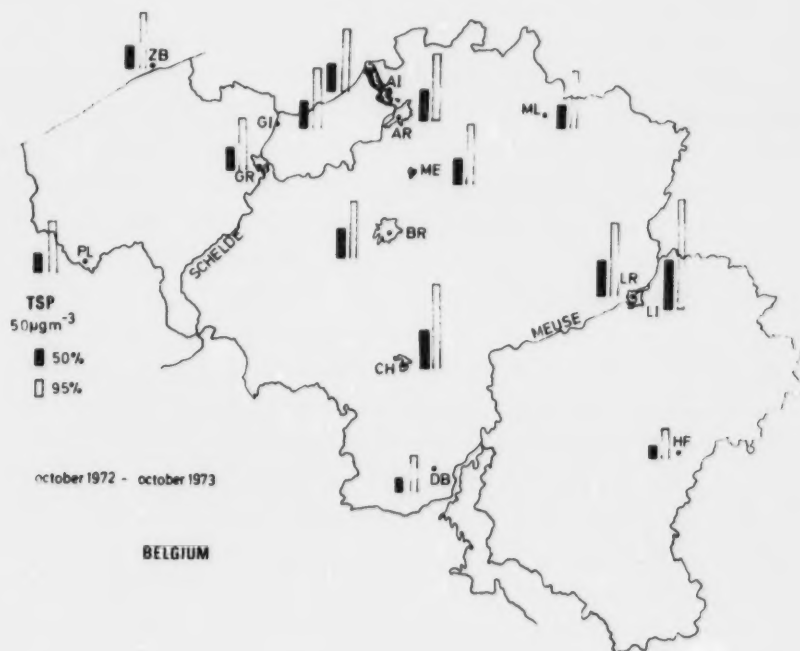


Fig. 1. Total suspended particulate matter at 14 stations in Belgium. Yearly means (50% and 95% percentiles) in $\mu\text{g m}^{-3}$.

The results suggest a generally high pollution level all over Belgium. Only 6 out of 14 meet the EPA primary ambient air quality standard for the U.S.A. ($75 \mu\text{g m}^{-3}$ as annual geometric mean). Atmospheric conditions such as ventilation, have of course an important influence

on the daily levels of the particulate material. At some sites however, local industrial emissions seem to dominate the general trend caused by meteorological parameters. In all stations, TSP levels strongly depend on wind direction. This is due to the fact that the ventilation varies generally with wind direction, low ventilation coefficients being nearly always associated with easterly winds. The TSP levels do not form a single log-normal distribution but they can be separated into two log-normal populations, one for wind directions from NNW to SSW and the other for the sector NNE - SSE. This is illustrated for the station PL in figure 2. Similar trends are found for the other stations.

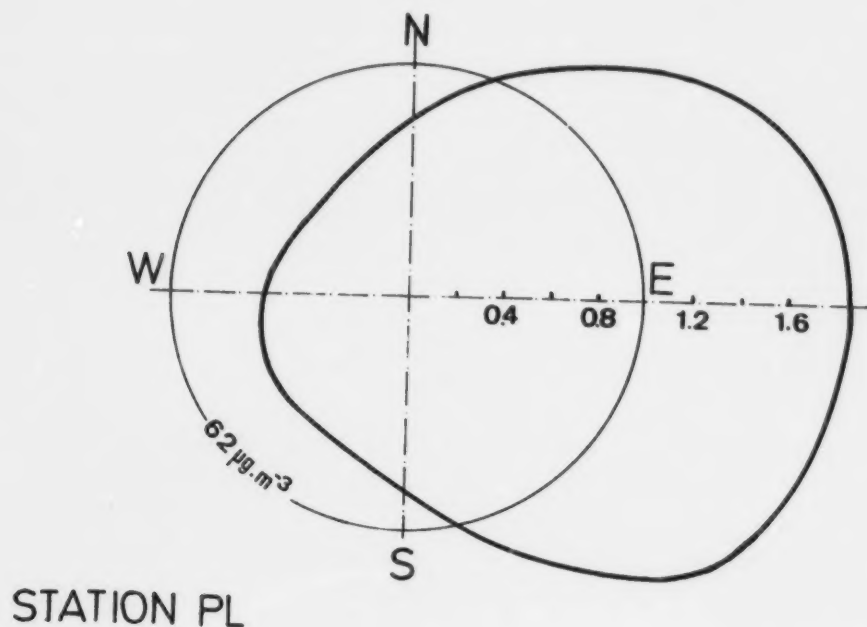
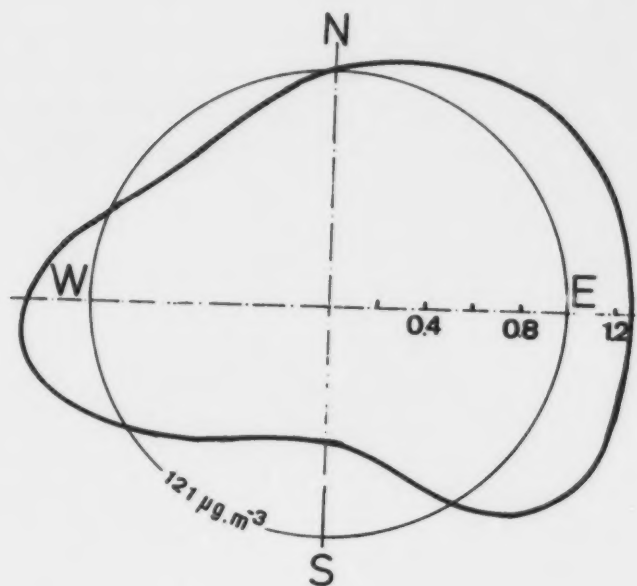


Fig. 2. Total suspended particulate matter as a function of wind direction, normalised to the yearly mean, at Ploegsteert (PL).

Important industrial contributions are recognised most easily in areas with intensive steel industry, such as the Meuse valley and the cities Liège and Charleroi. In figure 3, the mean TSP values for the different wind directions in the city of Charleroi are plotted. While the



STATION CH

Fig. 3. Total suspended particulate matter as a function of wind direction, normalised to the yearly mean, at Charleroi (CH).

relatively high values for the eastern sector can be explained as a result of the low ventilation, the high concentrations during westerly winds are due to contributions from steel mills west of the city. Other anthropogenic sources are more homogeneously distributed over the country and as a consequence their influence is not so obvious. If however the mean TSP values for the different days of the week are calculated a smooth pattern is obtained (figure 4). The results are roughly in agreement with the pattern of the daily electricity consumption which may be regarded as a measure of general human activity.

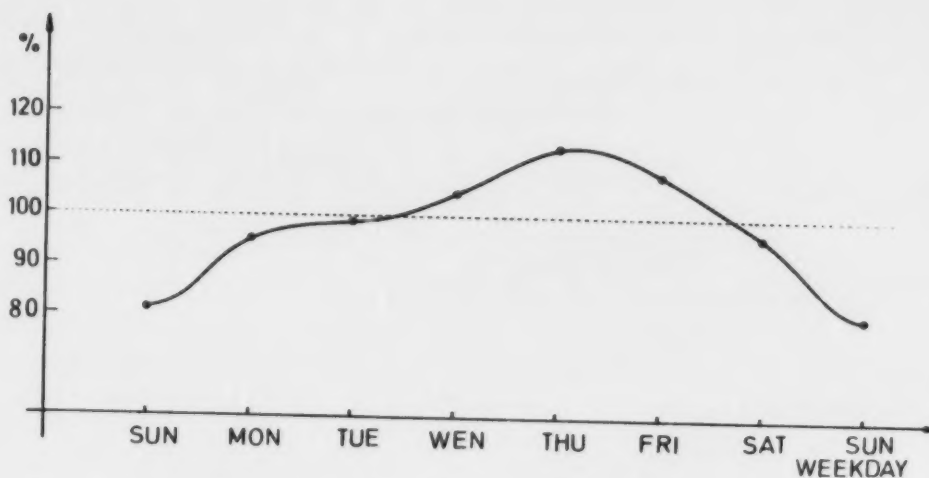


Fig. 4. Normalised weekly cycle of total suspended particulate matter averaged over one year at 14 stations.

3. Chemical Composition of Particulate Matter

The concentrations of most elements show larger local and daily variations than the TSP levels. Elemental ambient levels do not only depend on the particulate concentration, but specific emissions differentiate the composition of the dust. It was therefore preferred to compare particulate compositions instead of ambient air levels. In Table I the mean composition of the suspended particulate matter in Belgium is summarised. These arithmetic means are based on the analysis of 246 samples for most elements and of 14 samples for the components Si, F, Hf, Pb, SO_4^{--} , NO_3^- and NH_4^+ . As a measure for the constancy of these concentrations, the relative standard deviations are given. The concentrations of the majority of elements are relatively constant and similar to the concentrations in particulates collected at remote European sites (Rahn [8]). For all elements enrichment factors have been calculated as the ratio of the concentration in the aerosol to the concentration in crustal rock, normalised to the Si ratio (Mason [9]).

In spite of this similarity, inspection of the composition and enrichment factors still allows the elements to be grouped into classes with

TABLE I

Mean composition of aerosols collected at 14 stations in Belgium.
Relative standard deviation (S. D. %) and soil-enrichment factors (E. F.)
for all components determined

Ele- ments	Mean (ppm)	S. D. (%)	E. F.	Ele- ment	Mean (ppm)	S. D. (%)	E. F.
F *	2,970	98	31	Ag	10	131	1,000
Na	31,200	100	7.3 ***	Cd	340	231	11,000
Mg	5,440	85	1.7	In	12	428	800
Al	15,040	49	1.2	Sb	280	224	9,300
Si *	41,900	30	1.0 **	I	125	50	1,600
Cl	56,750	88	2,900 ***	Cs	9.5	98	20
K	14,700	54	3.7	Ba	1,220	143	20
Ca	29,700	58	5.4	La	18	66	4
Sc	4.0	48	1.2	Ce	30	64	3
Ti	1,180	95	1.8	Sm	1.75	92	2
V	480	54	23	Eu	0.52	81	3
Cr	240	126	16	Lu	0.76	186	10
Mn	1,830	102	13	Hf *	1.80	55	4
Fe	31,900	95	4.2	W	18	248	80
Co	39	185	10	Au	0.62	118	1,000
Cu	750	101	90	Hg	8.5	127	700
Zn	11,700	143	1,100	Pb *	10,500	71	5,300
Ga	43	79	20	Th	2.7	60	2.5
As	270	129	1,000	SO ₄ -- *	132,000	27	-
Se	60	115	8,000	NO ₃ - *	60,500	34	-
Br	2,370	74	6,300 ***	NH ₄ + *	36,400	43	-

* Based on a limited number of data

** Reference

*** Enriched by natural sea spray

similar behaviour. The first group contains the elements with small coefficients of variation and low enrichment factors namely Al, Si, K, Ca, Sc, V, I, La, Ce, Hf, Th and the components SO_4^{--} , NO_3^- , NH_4^+ . The nearly constant concentration of these elements in the aerosols suggests emissions by various diffuse sources whereas the enrichment factors in the vicinity of unity point towards emissions in soil-like ratios. Nearly all these elements belong to the geochemical class of the lithophile or oxyphile elements. In total they account for about 10% of the aerosol mass. The ions, often called secondary aerosols, amount to approximately 23%. The second group is composed of elements having slightly larger coefficients of variation and still low enrichment factors. Most of these elements have important industrial sources such as steel emissions (Fe, Mn, Cr, etc.), other anthropogenic sources (Br, F, etc.) or significant natural contributions (Na, Cl, Br, Mg). Although some of those elements have very intensive industrial and other anthropogenic sources, their enrichment factors remain low on the average. This is explained by the influence of steel mills and fly ash. These elements account for almost 15% of the total aerosol-mass and most of them are considered as lithophilic or siderophilic. The elements of the third group (Cd, In, Sb, Zn, As, Se, Ag, Au, Hg) have a larger enrichment factor and a relatively large coefficient of variation. Their major source is the non-ferrous metallurgy and some of them are of toxicological importance. All these elements are geochemically classified as chalcophilic. Although their enrichment factor in air particulates can be as high as 10,000, their total mass accounts only for less than 2% of the particulate matter. A summation of all the components determined in the aerosol reveals that only about 50% of the aerosol-mass is identified. The organic fraction, soluble in benzene, is 7.5% on the average and the particulate contains also about 5% water. The remaining 38% is probably organic material insoluble in benzene or carbon black. In Pasadena-aerosols, carbon concentrations of 20 to 45% have been found (Mueller et al. [10]).

By comparing the elemental compositions of the particulate matter collected at one or two stations but under different wind directions relevant informations concerning the location of major emission sources

can be obtained. An example of such a study is given in figure 5. The

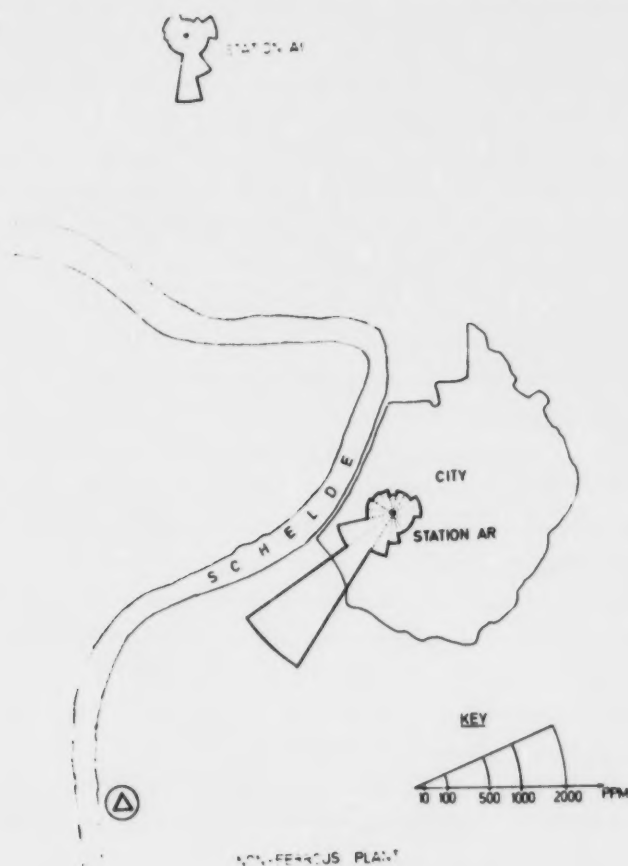


Fig. 5. Selenium concentration in the aerosol as a function of wind direction, at two locations in Antwerp. The concentrations are proportional to the areas of the sectors.

selenium concentrations vary strongly at stations AR and AI as a function of wind direction and point towards a large facility for non-ferrous metallurgy.

4. Mass-size Functions of the Elements

The distribution of the elements over the aerosol size range can give important indications about the nature of the source, the residence time in the air and the penetration and deposition in the human respiratory system (Hatch and Gross [11]). By means of Andersen cascade impactors the aerosols are separated in 8 fractions, with 50% cutoff diameters ranging from 11 to 0.43 μm and the even smaller particles are collected on a final filter. Figures 6 and 7 illustrate some results of such a measurement in an urban-industrial area (LR) and in a background area (HF). The elements can roughly be divided in three classes namely those with maximum concentrations on the giant particles ($> 3 \mu\text{m}$),

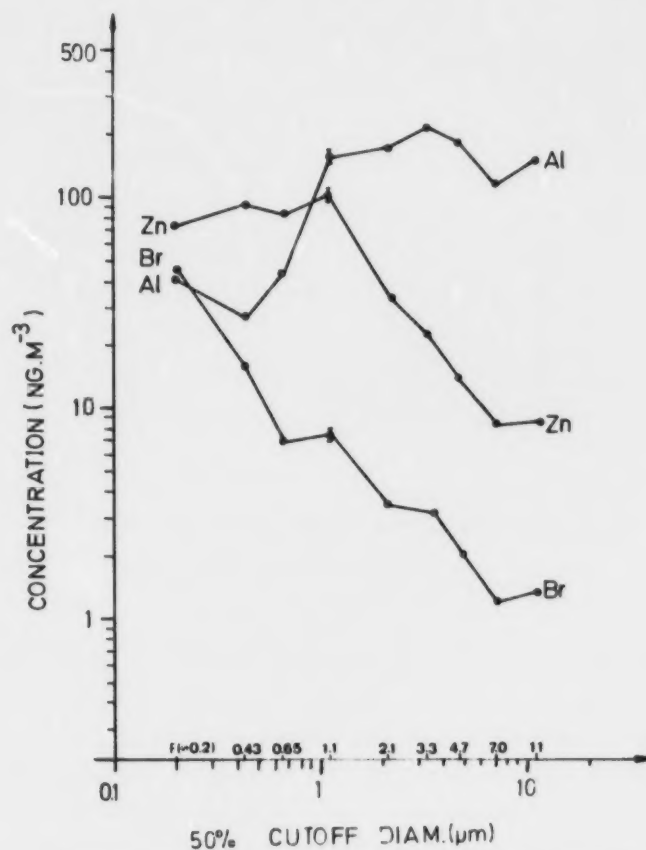


Fig. 6. Mass-size functions, as measured with Andersen cascade impactor at background station, Houffalize (HF).

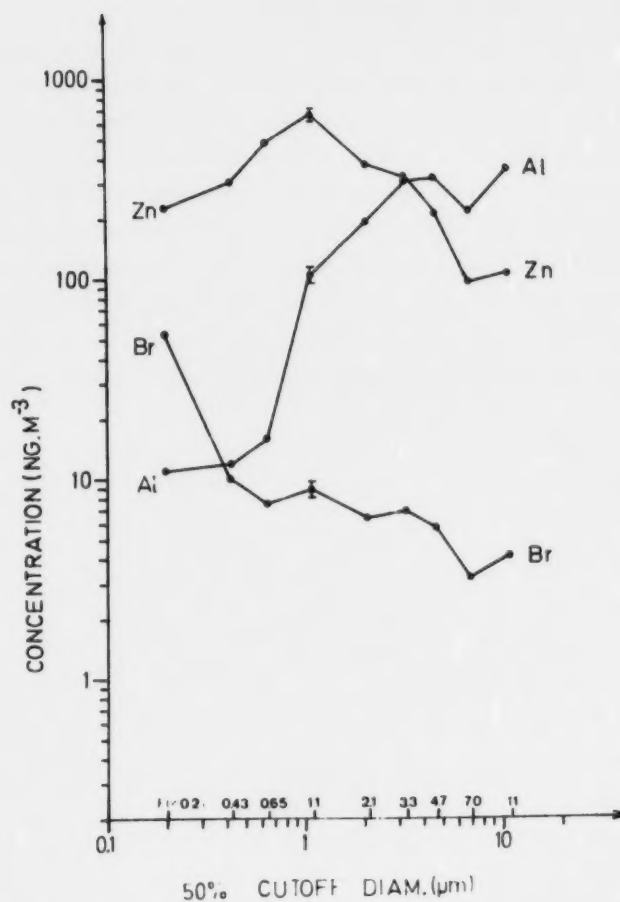


Fig. 7. Mass-size functions, as measured with Andersen cascade impactor at urban-industrial station, Liège (LR).

those with maximum concentration on the medium-sized particles (0.5-2 μm) and those mainly associated with the smaller particles ($< 1 \mu\text{m}$). The latter group shows generally a maximum concentration on the filter and consists of relatively volatile elements such as Se, As, Sb, V, Hg, Pb, Cl, Br and I. Condensation sources favour this kind of mass-size distribution. The elements on medium-sized particles such as Zn, Cd, In, Ag, Au are inhaled deeply into the lungs and have a relatively high

probability for deposition. The elements Al, Si, Ti, Fe, Ca, Mg, Th, Sc, etc. are generally produced by dispersion sources, which results in their association with the very large particles.

5. Conclusion

This short summary of a relatively large study illustrates that in Belgium the general pollution level of the aerosols is elevated in most areas of the country. The chemical composition of the aerosols varies as a function of location and as a function of wind direction. Especially the chalcophile elements show large concentration gradients, indicative of important emission sources. Their general association with the small particles makes them potentially hazardous. Since the elements can be divided in groups with common sources and similar atmospheric behaviour, a selected number of indicator elements can be found for each group.

ACKNOWLEDGEMENT

The N. C. S. L. V. (Nationaal Centrum voor de studie van Luchtverontreiniging door Verbranding) is greatly acknowledged for financial support.

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THE CHAMP AIR QUALITY MONITORING PROGRAM

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ABSTRACT

The CHAMP air monitoring system has been designed and installed to obtain short term, as well as long term, air monitoring data to assess the influence of pollutants on the health of five communities in the United States. The philosophy of design will be discussed with an emphasis on the techniques and methodology utilized to insure that the data obtained is valid. Program requirements, both present and anticipated, will be presented and the system as it now exists will be described.

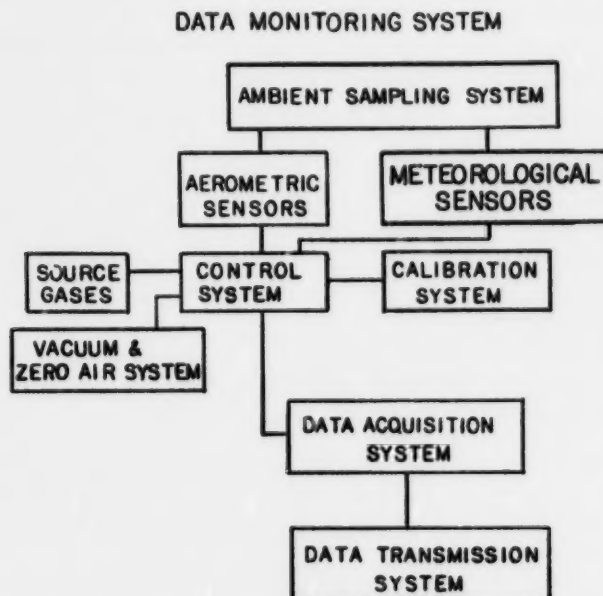
The Community Health Air Monitoring Program (CHAMP) system has been built to provide the Human Studies Laboratory of the Environmental Protection Agency (EPA) the physical data for its Community Health Environmental Surveillance System (CHESS). The objective of the CHESS program is to determine the health effects of ambient airborne pollutants on the population in order to establish realistic community air quality standards.

The CHAMP system is the product of an evolutionary growth of air quality monitoring which had its inception years ago. It is a product of the experience gained by EPA personnel in the air quality monitoring field coupled to the physical measurement skills developed within the aerospace community by the Rockwell International Science Center.

The system, at present, consists of 23 remote air quality monitoring stations located in five geographical areas within the United States, coupled to the central controller located at the National Environmental Research Center (NERC) at Research Triangle Park, North Carolina. This paper will describe the general features of the CHAMP system, stressing those features which we feel have made new contributions to the state-of-the-art.

A block diagram of the remote monitoring station is shown in Figure 1.

Figure 1



Block Diagram of Remote Monitoring Station

The sensors include aerometric pollutant analyzers, meteorological sensors, and a particulate sampling system. A major technical requirement of the program is to insure that all data obtained meets specific validity criteria. In order to meet this objective, each critical point in the measurement system is monitored. Each of the aerometric sensors employed must be calibrated at regular intervals; therefore, a dynamic calibration system has been included as part of the station; as the calibration directly affects the data validity, the critical elements of this subsystem are monitored.

Aerometric Sensors

At present the following sensors and measurement methods are used in the CHAMP stations:

OXIDES OF NITROGEN (NO-NO_x) - Determined by measurement of the light given off in the reaction of O₃ and NO. NO₂ is converted to NO prior to reaction and is determined by subtraction.

OZONE - Determined by measurement of the amount of light given off by the reaction of ozone and ethylene.

SULFUR DIOXIDE - Determined by measurement of the light emitted by sulfur atoms excited in a hydrogen-rich flame. The sample is pretreated to remove H₂S using a hot silver wire.

HYDROCARBONS - Methane is separated from other hydrocarbons in a gas chromatographic column. The hydrocarbon determination is made using a flame ionization detector.

PEROXYACETYLNITRATE, PAN - Separated utilizing a gas chromatograph. Determined utilizing an electron capture detector.

TOTAL SUSPENDED PARTICULATE - Determined using a High Volume sampler equipped with a flow controller.

SIZE SEPARATED PARTICULATE - Determined by filter impaction after size separation utilizing a 20 micron impactor following by a 3.5 micron impactor.

In addition, the following parameters constitute the primary data:

- Wind Speed
- Wind Direction
- Barometric Pressure
- Relative Humidity
- Ambient Temperature

These are measured using standard meteorological sensors with the exception of the relative humidity sensor which utilizes a solid state semiconductor surface.

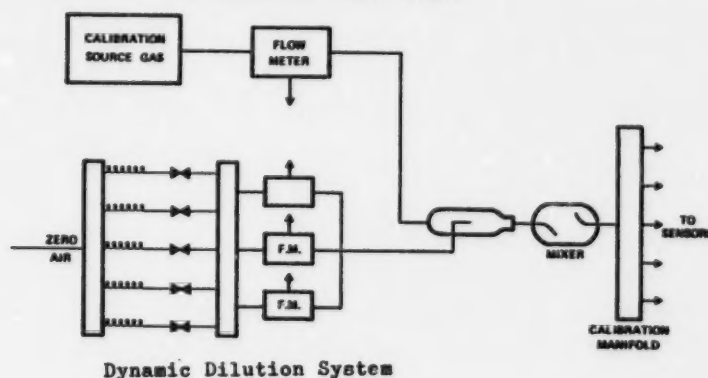
Each aerometric sensor has been modified to permit electrical readout of the complete operational status of the unit. These status indications include power supply on/off, range, etc. In addition, each critical flow within the analyzer is monitored; examples include hydrogen flow in the SO_2 analyzer, sample and ethylene flow in the ozone analyzer, sample and oxygen flow in the oxides of nitrogen analyzer, etc. All other points which affect the validity of the data are monitored. These include sample inlet flow, valve status, internal temperature of the shelter, etc.

Aerometric Sensor Calibration Subsystem

As indicated above, a complete dynamic calibration subsystem is provided in each station. This system has been designed to provide multipoint calibration capabilities of each aerometric analyzer.

Maintenance of calibration sources at the low concentrations required is extremely difficult, if not impossible. This is due to reaction and irreversible adsorption of the pollutant gas on the walls of the cylinders. We, therefore, have utilized sources at reasonably high concentrations and have provided a dynamic dilution system as shown in Figure 2. The design objectives for the calibration system include precision which is superior by at least a factor of five to the instrument being calibrated and the ability to implement, at a later date, a fully automated calibration capability. It was, therefore, decided at the beginning to utilize mass flow sensors throughout; these provide significantly improved flow measurement over visually read rotometers, as well as the ability to permanently record the calibration process itself.

Figure 2
CALIBRATION SUBSYSTEM

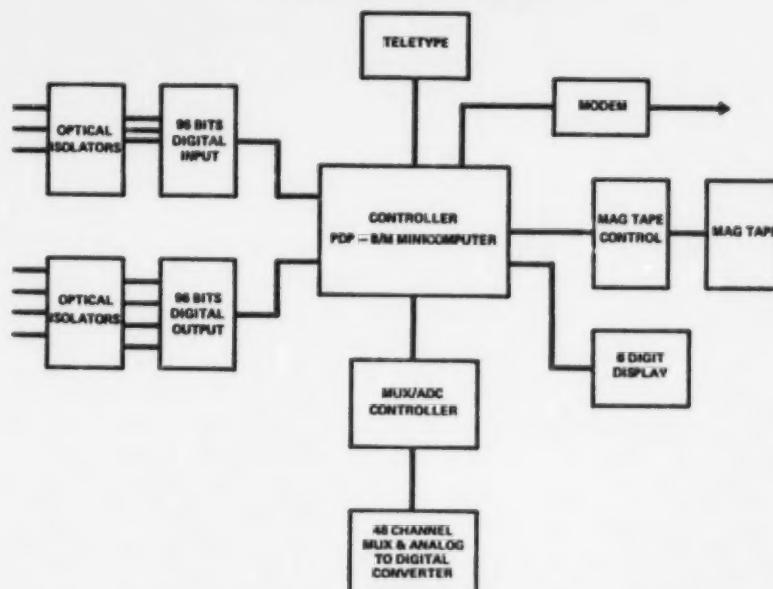


Data Acquisition System (DAS)

The fundamental improvement in the CHAMP monitoring system in this area is the utilization of a minicomputer as the primary logical element of the system. A block diagram of the CHAMP DAS is shown in Figure 3. We have employed a Digital Equipment Corporation PDP-8/M minicomputer with 16K of core, hardware multiply/divide, power fail/auto restart, a 60 Hz real-time clock, and a modem interface. The minicomputer is interfaced to a Pertec 9-track, 800 bpi magnetic tape, a Xincom multiplexor/ADC, a digital display unit, 96 bits of digital input, and 96 bits of digital output.

Figure 3

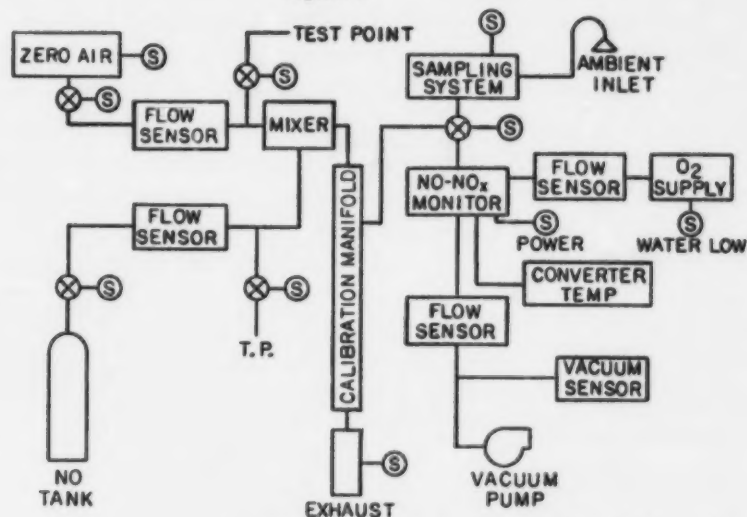
DATA ACQUISITION SET



CHAMP Data Acquisition System

The utilization of the minicomputer in the station permits a highly flexible mode of operation. One of the prime objectives of the program is to acquire data which can be validated. The term "valid" implies that all aspects of the remote station operation are functional and within tolerance. The implementation of this concept is shown in Figure 4 for the oxides of nitrogen analyzer. This instrument operates on the principle of measuring the amount of light emitted by the chemical reaction $\text{NO} + \text{O}_3 \rightarrow \text{NO}_2 + \text{O}_2 h\nu$.

Figure 4



Oxides of Nitrogen Sampling and Calibration Subsystem

Nitrogen dioxide is determined by conversion to NO using a carbon reactor at 240°C followed by the chemiluminescent determination of NO. The critical parameters of the analysis are:

1. Reaction chamber pressure. The chemiluminescent reaction sensitivity is a function of the chamber pressure.
2. Converter temperature.
3. Sample flow rate.
4. Oxygen flow rate. Oxygen is utilized to synthesize for the reaction. A constant flow is required.

Each of these critical parameters is continuously monitored to insure that the data is indeed valid. In addition, the position of each valve is monitored in order to insure that sample and reactant flows are properly routed.

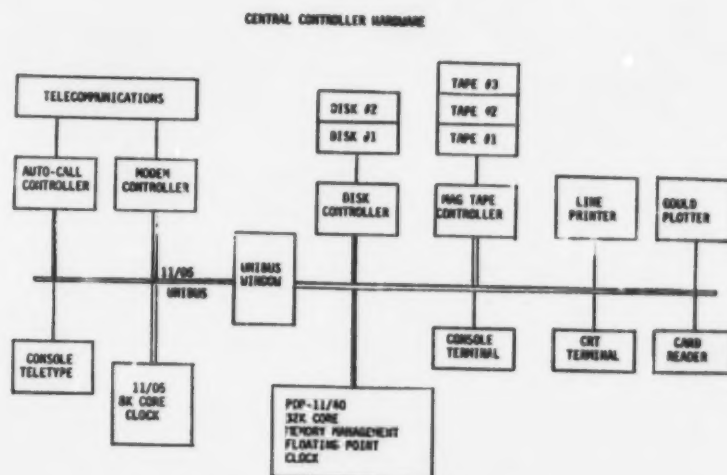
This philosophy of design has been used throughout the CHAMP analysis system. As each datum is acquired, it is stored on the magnetic tape (9-track, 800 bpi). These data are then transmitted to the central controller at Research Triangle Park, North Carolina for validation and analysis. In addition to the primary task of data acquisition, the local minicomputer has been programmed to act as an aid to the operator. Upon command from the teletype, the operator can obtain a printout of the status of each instrument; a log of all current values measured in physical units, etc. The computer also monitors the calibration of each instrument to insure that it

has been properly performed. The operator can also control the operating parameters for each instrument; these include the averaging time and the calibration constants.

At present, the system consists of 23 remote stations located in Southern California, Utah, New York, Birmingham, Alabama, Charlotte, and Research Triangle Park, North Carolina. Each can be individually interrogated by a central controller via dial up voice grade lines. The remote station is equipped with a full duplex, two wire autoanswer modem. Full duplex operation is achieved by utilizing 1200 baud forward (remote to central) transmission and 150 baud reverse (central to remote) transmission. The data is transmitted in 512 byte blocks with byte parity and record checksums. Retransmission is utilized if a communication error is found.

The central controller consists of a dual processor system, configured of a PDP-11/05 connected to a PDP-11/40 via a "bus window". The configuration was chosen to provide for rapid communications processing simultaneously with batch processing of the data. A block diagram of the central controller is shown in Figure 5. The central controller has been provided,

Figure 5



Block Diagram of Central Controller.

principally, as a means to aid in validation of the physical data as it is received. The validation procedure consists of checking that the various critical instrument parameters are within tolerance, that the various valves are correctly set, and that the calibrations of the instruments have been

made at the proper interval. In addition, the controller is utilized to store recent data for comparison checks, property location control, etc.

Overall validity of the data of a long term requires a systematic quality assurance program. Such a program has been implemented for the CHAMP system. A full five point calibration is given each aerometric analyzer every two weeks. Other sensors are calibrated at periods consistent with the known drift and failure rate of the device. An archive of each instrument's performance is kept in order to track degradation and systematic problems.

Each calibration source is certified by two independent means in the laboratory. Source gas tanks are rechecked every three months to insure that degradation has not taken place. Each station is visited by quality assurance personnel at irregular intervals to establish that the local operator is performing the normal routine maintenance tasks required.

In conclusion, the CHAMP system provides the EPA the tool by which aerometric data for the CHES program can be obtained. By utilization of state-of-the-art technology, much of it derived from aerospace experience, the validity of the data is enhanced, thus establishing a high confidence factor for any air quality standards derived from the program.

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STUDIES OF TRACE SUBSTANCES IN AN URBAN ATMOSPHERE

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ABSTRACT

An investigation has been undertaken of certain trace substances in the atmosphere of New York City in order to: 1) improve our understanding of the seasonal and year-to-year variations in the concentrations of these substances; 2) ascertain their particle size distribution; 3) determine the extent to which human tissue burdens are due to atmospheric exposure; and 4) enable one to apportion the total suspended particulates among some of the major sources, such as space heating, power generation, ocean spray, and automobile traffic. In addition, certain characteristics of settled dust have also been studied in order to understand the relationship of settled to airborne dust and to develop methods by which the source of settled dust can be ascertained through analytical procedures. This paper summarizes the findings to date, with particular emphasis on the new methods that have been developed in the course of our study.

1. Introduction

A study of the composition of the urban aerosols of New York City has been undertaken in the hopes of achieving better understanding of the sources, distribution, and fate of aerosols in the urban environment. The overall objectives of this program are 1) To use the physical and chemical properties of suspended and settled dusts to characterize their sources. 2) To ascertain the extent to which trace elements present in suspended dust are absorbed by New York City residents.

In order to achieve these objectives we have undertaken to:

- a) Determine temporal patterns in the variation of trace metal and ion concentration in total suspended particulate (TSP) and settled dust.
- b) Establish the effects of meteorological parameters on the TSP and trace element concentrations.
- c) Define the sources of the trace metals or ions.
- d) Relate the aerosol trace element compositions to human tissue burdens.

A system for sampling airborne particulates is in use that is capable of continuous operation for 7 days at a constant flow rate of $0.57 \text{ m}^3/\text{minute}$. From 1967 through 1970, and 1972 through 1973, samples have been collected at 4 locations for analysis by atomic absorption spectrophotometry as reported by Kneip, et. al. [1]. By use of weekly rather than daily samples, short-term fluctuations were successfully averaged out, with a substantial reduction in sampling load.

In addition, sampling of dustfall was initiated in 1972. Weekly samples from each of the four stations are analyzed for 9 metals, and monthly composites are analyzed for 4 to 6 additional elements or ions. (Table I) Monthly dustfall samples are analyzed for all of these materials. Methods to quantitatively analyze trace element concentrations in sus-

TABLE I
ELEMENTS ANALYZED IN AIR FILTER SAMPLES

<u>Element</u>	<u>Standard Deviation (%)</u>
<u>WEEKLY</u>	
Cadmium	10
Chromium	18
Copper	11
Iron	22
Lead	2
Manganese	7
Nickel	8
Vanadium	14
Zinc	3
<u>MONTHLY</u>	
Calcium	-
Magnesium	-
Potassium	-
Sodium	-
Chloride	-
Nitrate	-

pended particulates, settled dust and human tissue specimens were restudied to obtain increased accuracy and sensitivity and improved precision. These methods were tested using available National Bureau of Standards reference materials.

2. Experimental

Weekly samples of suspended particulates are collected at four locations in New York City and one location in a rural area. The locations and characteristics of these stations are given in Table II. Station No. 5, which has been installed in Sterling Forest, about 40 miles northwest of New York City, is on a hill about 1 mile from the nearest road and should serve

TABLE II
LOCATIONS OF SAMPLING SITES

<u>Station</u>	<u>Address</u>	<u>Region</u>	<u>Height Above Street</u>
1	376 Hudson St. (Houston St.)	S.W. Manhattan	13 stories
2	500 First Ave. (30th St)	East Side of Manhattan	14 stories
3	Sedgewick Ave. (near Fordham Rd)	Western Bronx	3 stories
4	Kissena Blvd. (near 69th Rd)	North Queens	4 stories
5	Long Meadow Rd	Tuxedo, N.Y.	700' above road level

as an indicator of the background level of the aerosols entering the New York City area on northwest winds.

Samples are obtained by drawing air through a 10.5 cm x 25.4 cm glass fiber filter with a Roots-Connorsville pump. The flow is controlled at 0.57 m³/min by use of a by-pass valve actuated by a feedback loop to maintain a constant pressure drop across an orifice which is in line with the sampling head.

A section of about 45 cm² is cut from the filter which has a total exposed area of about 406 cm². The fraction taken as the sub-sample is determined by a weight fraction technique. The metals are dissolved by wet ashing in a nitric-perchloric acid mixture (4:1) to the first appearance of perchloric acid fumes.

3. Results and Discussion

3.1 TSP and Composition Data

The samples of the New York City aerosol have been analyzed in this way for eleven trace metals previously listed in Table I. The precisions given in the table were obtained by analysis of replicate portions of the 10.5 cm x 25.4 cm glass fiber filters and include the variance due to sampling, sub-sampling, sample preparation and analysis.

The general trends in the metals concentrations are shown in Table III for Stations 1, 2 and 3. Decreases have been observed for copper, chromium, lead and manganese as well as vanadium in the 1969-1973 period.

TABLE III
TRACE METALS IN SUSPENDED PARTICULATES
AT STATION 1, STATION 2, AND STATION 3
ANNUAL GEOMETRIC MEANS (ng/m³)

STATION 1

Element	1968	1969	1972	1973
Pb	2990	1900	1390	1143
V	1000	564	81	169
Cu	212	187	152	95
Cr	63	42	28	22
Fe	-	-	1301	1723
Mn	71	61	45	55
Na	2380	490	498	634
Ni	-	-	29	58
Cd	23	11	16	9

STATION 2

Pb	-	2100	1361	1193
V	-	874	59	68
Cu	-	526	45	62
Cr	-	33	11	7
Fe	-	-	1332	1281
Mn	-	89	26	31
Zn	-	670	350	416
Ni	-	-	28	67
Cd	-	10	5	5

STATION 3

Pb	3820	2760	1880	1520
V	1230	795	48	67
Cu	133	45	48	43
Cr	49	23	5	4
Fe	-	-	1590	1310
Mn	54	40	27	31
Zn	730	1120	232	273
Ni	150	122	127	221
Cd	14	9	4	3

The TSP levels in the city have shown a general decline as noted in the data of Table IV. Current annual means have declined to less than $90 \mu\text{g}/\text{m}^3$ and one site (Station 3) reached the primary quality goal of $75 \mu\text{g}/\text{m}^3$ in 1973.

TABLE IV
TOTAL SUSPENDED PARTICULATE 1968-1973
ANNUAL GEOMETRIC MEANS $\mu\text{g}/\text{m}^3$

	<u>1968</u>	<u>1969</u>	<u>1972</u>	<u>1973</u>
STATION 1	125	104	-	-
STATION 2	-	134	79	81
STATION 3	113	108	79	75

The concentration of vanadium has dropped by an order of magnitude during this same period as shown in Figure 1. From 1968 through 1969 the airborne V concentration decreased by about one-third to one-half as compared to a reduction of 50% in the sulfur content in fuel oil burned for space heating. During this period, Consolidated Edison was required to burn residual fuel oil with no more than 1% sulfur, while oil used for space heating was reduced gradually from 2.2% S to 1.0% S. From 1969 to 1973 a further drop occurred with airborne vanadium falling in 1972-73 to one-tenth the 1968 levels. Fuel sulfur contents in 1972-73 were restricted to 0.3% for heating oils and 0.5% for power station usage.

3.2 Meteorological Factors

The ambient concentration of a pollutant in the atmosphere depends on the nature of its source, its dilution or dispersion by atmospheric motions, and its rate of removal from the atmosphere by washout in rainfall and by direct impingement onto surfaces. If one is to use observed trends in airborne trace metal concentrations as indications of changes in source emission characteristics, it is necessary to compensate in some way for variations in the meteorological phenomena

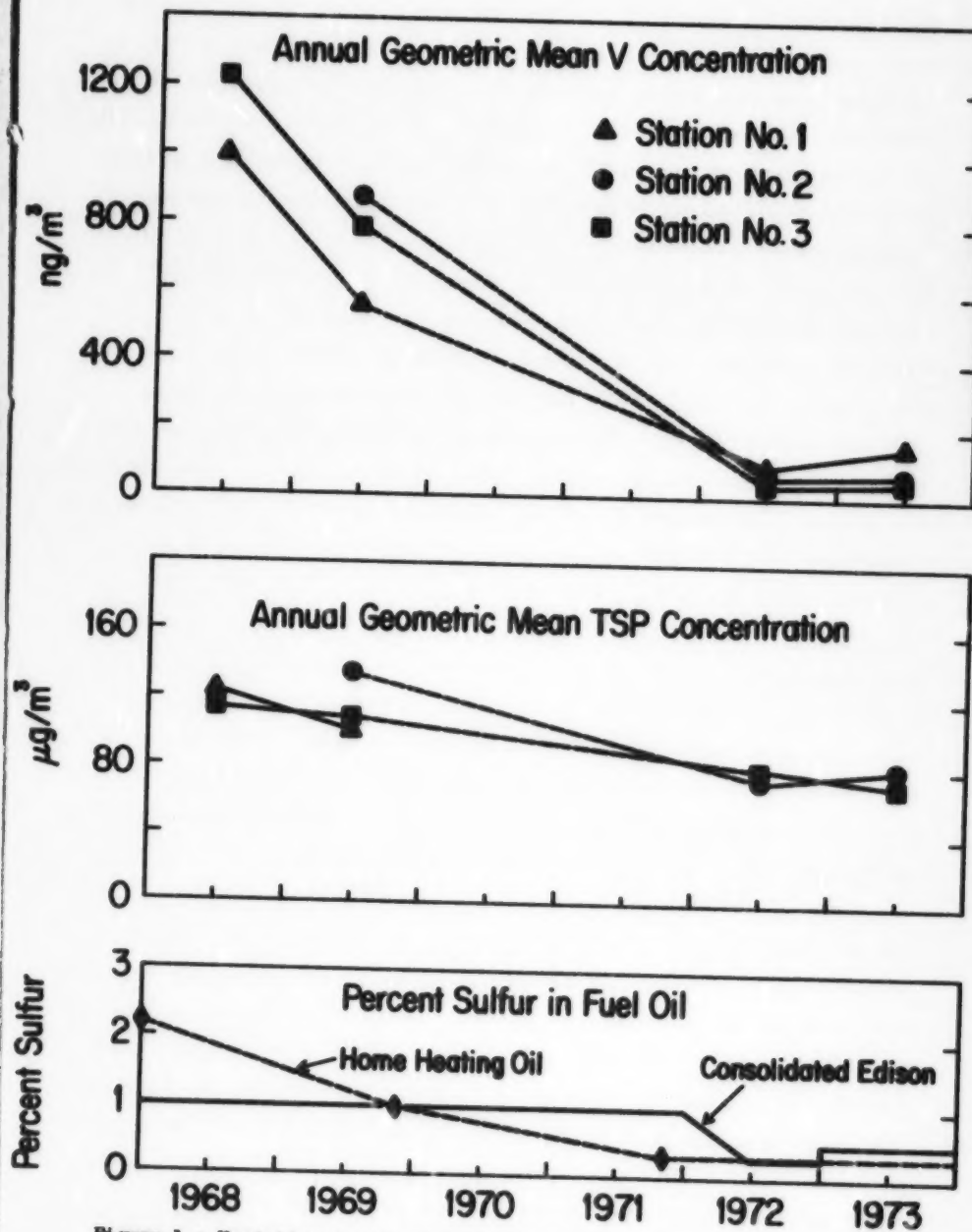


Figure 1 : Variation in the atmospheric concentration of vanadium (V) and total suspended particulates (TSP) as well as in the concentration of sulphur in fuel oil in New York city for the period 1968-1973

as reported by Rubin [2] . The meteorological factors which seem most important for this purpose are precipitation, which relates to atmospheric scavenging processes as reported by Engleman [3]; wind direction, which is important in evaluating emissions from major point sources; and wind speed and mixing depth as reported by Holzworth [4], which relate to atmospheric dispersion processes.

We have used seasons related to heating needs in our studies rather than calendar seasons, so that Winter is December, January and February; Spring is March, April and May; Summer is June, July and August; and Fall is September, October and November. No consistent rainfall pattern has been found as a function of season. For this reason we have, for the moment, postponed detailed examination of the effects of precipitation on observed concentrations of airborne metals and particulates. The degree to which pollutants diffuse vertically depends to a great extent on the vertical temperature gradient of the atmosphere. In New York City, this profile is determined daily, shortly after sunrise, using balloon-borne temperature and altitude sensors which relay information to ground based stations. Using the method described by Holzworth [4], these profiles can be used to calculate the height to which mixing will occur.

Daily dispersion factors were computed for this study as the product of the mixing depth and the wind speed. Average weekly values for mixing depth, wind speed and dispersion factor were examined and both wind speed and mixing depth were found to exhibit seasonal variations, being lower during the summer and higher in the winter. The week-to-week variations are large and the indulging pattern is difficult to visualize in unsmoothed data. Four-week moving averages of the dispersion factor show a very distinct pattern, with a definite minimum during the summer and maximum during the winter months.

This pattern has significance in that during periods of high dispersion, the concentration of airborne pollutants from relatively constant sources would be reduced because of dilution effects. During periods of low dispersion, as during the summer months, pollutant concentrations would appear to be increased even though source emission rates were unchanged.

A means of compensating for this variable dispersion is to normalize particulate concentrations to a constant dispersion factor. The TSP and trace metal data for the period February 1972 to March 1973 have been normalized to a constant dispersion factor of $3100 \text{ m}^2/\text{sec}$, the average factor for 1972, by multiplying the concentration by the monthly dispersion factor and dividing by 3100.

The effect of this transformation on the data is clearly shown by several seasonal shifts. For instance, peak values for Total Suspended Particulate shift from the summer to winter. This indicates that an important source of particulate emission during the winter months is obscured by the effect of the dispersion factor. It is reasonable to assume that space heating is such a source. Support for this hypothesis is found in the record of degree days. TSP values as a function of degree days (7 day weekly averages) indicates that these two variables are strongly correlated, ≤ 0.001 . The winter peak in the normalized TSP concentration evidently reflects the increased emissions from space heating.

Based on these results and the assumption that other sources remain constant over the year, a baseline average was estimated from the summer results and this average subtracted from weekly winter TSP values to estimate the magnitude of the heating systems as sources. These calculations show that heating emissions contribute 20% of the annual average TSP with the highest weekly fraction estimated at 60%.

The data for lead, vanadium and copper have also been examined in "as is" and in dispersion normalized forms. The

results for copper show no significant seasonal relationships both before and after normalization. The corrected values for vanadium show effects similar to those for TSP with more distinct winter peaks after normalizing. The lead data show no seasonal relation before normalizing, however, the normalized values are distinctly lower during the summer, a period when schools are closed and many people take vacations. No quantitative detailed traffic analyses are available, but qualitative observations from many sources agree that the summer is a period of significantly lower traffic.

Dispersion normalization of the TSP and metals data appears to offer a means of obtaining correlations between such data and source emissions free of variations caused by the variable meteorological conditions from season to season.

3.3 Source Related Trace Elements

One of our major interests in the trace element pollutants in urban aerosols stems mainly from the need to achieve a better understanding of the sources of urban particulate pollutants. Larsen [5] estimated the total contribution of the automobile to the Boston aerosol through a study of lead and other aerosol components from an automotive tunnel. More recently, Kneip et. al. [6] and Friedlander [7] have examined the relationship between aerosol composition data and source contributions.

The tracers expected to be of use are sodium and chlorine for sea salt; calcium, aluminum, silicon and potassium for soil; lead for automotive sources; vanadium and possibly nickel for fuel oil (principally residual); and copper, zinc, chromium and others as industrial tracers. Based upon the emission inventory and source sampling data in the literature we have selected the following five elements as probably associated with the major sources of the urban aerosol.

The literature values for source terms for each of these elements were evaluated to determine the similarity of the sources to those in the system under study, and therefore the likelihood that these terms would be representative for our study and values selected as preliminary source term factors as given in Table V. As sampling and analysis of sources was prohibitively expensive, a mathematical technique has been developed to confirm the factors selected. The method and results were discussed previously by Kneip [6].

TABLE V
TRACER ELEMENTS CHARACTERISTIC
OF SELECTED EMISSION AEROSOL SOURCES

<u>Element</u>	<u>Associated Source</u>	<u>Element Fraction in Source Aerosol</u>
Pb	Automobile	0.09
V	Fuel Oil Burning	0.047
Cu	Incineration	0.01
Na	Sea Salt Aerosols	0.33
K	Soil Particulates	0.024

Using the literature values for the concentration of each element in the aerosols emitted by the sources, a matrix is solved to establish the fraction of each of the elements attributable to the individual sources. These fractions are then used in a correlation-regression analysis to recalculate the source terms of the elements for each aerosol source as coefficients in the equation obtained by combining and rearranging equations as follows:

$$TSP = \sum_j E_j$$

$$F_{ij} = \frac{f_{ij} \times E_j}{C_i}$$

$$E_j = \frac{F_{ij} \times C_i}{f_{ij}}$$

$$TSP = \sum_{i,j} \frac{1}{f_{ij}} \times F_{ij} \times C_i$$

j = an individual source

i = a selected element

E_j = ambient concentration of aerosol associated with the source j

F_{ij} = Fraction of airborne concentration of element i associated with the source j

f_{ij} = Fraction of element i in aerosol from source j

C_i = Concentration of element i in $\mu\text{g}/\text{m}^3$ in the ambient aerosol.

The sources chosen must account for the total amount of each of the elements selected, and the TSP total must be a summation of the sources under study.

What we are attempting at this point can be expressed as follows. We have assumed that there are six contributors to the TSP. These are automobiles, fuel burning (for both space heating and power production), incinerators (both municipal and apartment house), suspended particles of soil, salt spray and particles from undefined industrial and commercial sources (labelled for convenience "other"). The particles associated with the first five of these sources can be traced by certain elements: Pb, V, Cu, K, and Na, respectively.

The multiple regression solution to the equations shown above essentially tries to account for changes in the TSP from week to week in terms of changes in the selected metal concentrations. That portion of the TSP variation which is unrelated

to changes in the metal concentrations is attributed to changes in the undefined sources (others). From this relation using the fractions of each element due to the various sources (F_{ij}), we can obtain recalculated values for the element fractions (f_{ij}).

These fractions for element composition in emitted aerosols, as generated from actual ambient aerosol compositions, can then be used to calculate the aerosol mass associated with each source and the apparent percentage that each source contributes to the total aerosol. No significant change in the calculated element fractions (f_{ij}) is found upon successive recalculations indicating a satisfactory fit of the data to the equations in use. The results for these fractions are given in Table VI. The results for the source contributions to the ambient TSP are given in Table VII.

TABLE VI
ELEMENT FRACTIONS CALCULATED
FOR ASSOCIATION TO SELECTED SOURCES

Element	Related Source	Element Fraction (f_{ij})		
		Station 2	Station 3	Pooled Data
Pb	Auto	0.055	0.076	0.097
Cu	Incineration	0.013	0.051	0.012
V	Fuel Oil	0.008	0.006	0.005

TABLE VII
PERCENT OF TSP ASSOCIATED WITH ELEMENT

Element	February - August 1972	February 1972 - January 1973		
	Medical Center	Medical Center	Carpenter Hall	Combined Data
Pb	32	31	32	22
V	11	10	11	14
Cu	4	5	1	4
Na & K	17	(18)	-	-
Other	37	54 (36)	55	59

() Values estimated on the assumption that the February-August contribution was unchanged.

These percentages represent the fractions of the TSP which can be mathematically correlated to the variations in composition as discussed. This method associates the TSP with the ambient aerosol, not the actual aerosol emitted by the source. Thus, agglomeration, attachment, condensation, impaction, or other causes of growth or dispersion of particles have already occurred prior to the measurements used in these calculations. Moreover, the association between Pb and 20-30% of TSP may result from the fact that Pb is present in automobile exhaust and that automobiles generate dusts in a variety of ways, including abrasion of brake linings, tires and road surfaces, or comminution and resuspension of settled dust on street surfaces.

The data do provide a means of judging the probable importance of further examination of each source. For instance the estimates for vanadium related aerosols show a total of 10 to 14% of the TSP as related to oil burning sources. We have estimated that space heating contributes about 20% of

the TSP at Station No. 2 during 1972 based on the "excess" normalized TSP observed during the winter heating season. This result compares well with the estimates of 10 to 14%. It appears that further reductions in these emissions are not likely to be productive if concentrated on the large power stations burning residual fuels, but must include efforts to reduce the emissions related to the heating systems in the city. As a definite winter peak occurs in the TSP, such efforts may be crucial in reaching a $75 \mu\text{g}/\text{m}^3$ annual mean.

3.4 Particle size distributions

To obtain information about the particle size spectrum of the urban aerosol, our colleague, Morton Lippmann, has designed a size selective particle classifier which will enable long-term sampling of large volumes of the urban air. Analyses of these samples will permit correlation of trace metal concentrations as a function of particle size and permit comparisons to emission source characteristics and meteorological data.

The device uses an array of size selective centrifugal separators (cyclones) as precollectors in four-parallel, two-stage systems using glass fiber filters for the second stage. This type of cyclone has been in use for short-term "respirable" dust sampling in industry, but until now has not been incorporated in a long-term urban aerosol particle size collector. The air is moved by an integral motor-blower units (Radeco # 809V). The cyclones collect particles larger than the selected particle size cut while the filter papers collect particles smaller than the selected particle size cut. One filter is used with no precollector to provide a total value independent of constant flow sampler. By carefully adjusting the inlet geometries to get equal inlet velocities, it has been possible to get reasonable agreement of TSP and the sums of the weights for the two stages in each classifier. The

TSP values obtained by our constant flow sampler and the array of particle size classifying samplers are given in Table VIII. The 3.5 μm stage has given high total flows due to a flow control problem from the low speed setting used to obtain the 3.5 μm cut. A new feedback circuit will be used which will afford improved control and lower the total flow to the desired value.

TABLE VIII
TOTAL SUSPENDED PARTICULATE
FROM SIZE SELECTIVE STAGES

<u>Sampler</u>	<u>Mass collected ($\mu\text{g}/\text{m}^3$)</u>	
	Run 1	Run 2
Constant Flow		
0.3 m ³ /min	114	Lost
Total Stage	115	110
50% 3.5 μm	142	130
50% 2.5 μm	118	No Sample
50% 1.5 μm	121	100
50% 0.5 μm	101	103

3.5 Dustfall

Monthly samples of dustfall collected at these stations in New York City have been analyzed for Cd, Cu, Cr, Fe, Mn, Ni, Pb, V, and Zn. Two years of data do not disclose any discernable trends in the data as a function of time. A preliminary attempt to correlate dustfall levels with rainfall has not been fruitful. For example, although November 1972 had twenty times the precipitation as August 1972, there was no significant difference between the masses of the trace elements deposited ($P \leq 0.05$).

The month-to-month variability in the values for most of the elements is large. Because of this a great deal of addi-

tional data will be needed if seasonal trends are to be delineated.

3.6 Deposition Velocities

The deposition velocity is defined as the particle deposition flux to a surface divided by the particle concentration above that surface. Thus, μg of particles/ cm^2/month , deposited in a dustfall collector, divided by the average concentration of particulates in air measured during that month, in units of $\mu\text{g}/\text{m}^3$, multiplied by a dimensional constant of 0.38 yields deposition velocities in units of cm/sec . Average deposition velocities calculated for each metal are shown in Table IX along with particle size estimates based on a Stoke's Law approximation and an assumed particle size of $0.5 \mu\text{m}$ for lead.

TABLE IX
AVERAGE DEPOSITION VELOCITIES
AND ESTIMATED PARTICLE SIZES

<u>Element</u>	<u>Average Deposition Velocity (cm/sec)</u>	<u>95% Confidence Range of Apparent Particle Size, MMD (μ)</u>
Lead	0.65 ± 0.08	0.46-0.52
Nickel	1.34 ± 0.26	0.64-0.78
Cadmium	2.59 ± 0.58	0.87-1.08
Vanadium	2.41 ± 0.17	0.92-0.99
Zinc	3.85 ± 0.90	1.06-1.35
Iron	4.70 ± 1.06	1.18-1.48
Manganese	5.71 ± 0.95	1.34-1.60
Copper	7.04 ± 0.76	1.76-1.83

3.7 Trace Elements in Human Tissues

Analysis of human tissues has been undertaken to improve the knowledge of the relationships between trace metal-tissue distributions and the various routes of exposure, with particular emphasis on the urban aerosol source. The tissue distribution of the elements in various tissues generally agree with the values reported by Tipton [8]. Lead, nickel and chromium have been found to show elevated levels in the combined Hilar and pulmonary lymph nodes as compared to the lung. This distribution which indicates a phagocytic clearance mechanism, and a clearance half-time of 39 days for lead from our data are in qualitative agreement with the fact that we find lead in the New York aerosol to be less than 20% soluble in water.

4. Conclusions

These studies have provided data on the concentrations of trace elements in the aerosol to which residents are exposed in New York City. Correlations of the composition and TSP variations have shown associations to exist between lead, vanadium, copper, sodium and potassium and some 40% to 65% of the total aerosol. The aerosol associated with lead (and possibly the automobile) accounts for 20 to 30% of the total, while that associated with vanadium (and probably oil burning sources) accounts for 10% to 14%. A further effort must be made to determine whether other major source correlations can be found in the remaining aerosol currently attributed to "other" sources.

A means has been evaluated for correcting for meteorological variations and TSP and metal concentrations have been normalized to constant mixing conditions. The results have revealed distinct source-related seasonal variations which had been partially or wholly obscured by the variations and interactions in the meteorological factors. Vanadium, lead and TSP show maxima and minima in the normalized data which now can be

related to source terms independent of the variable meteorological effects. The normalized TSP and vanadium results clearly reflect space heating and closely correlate mathematically to degree day data. The annual space heating contribution has been calculated to be about 20% on an annual basis from these results and is in fair agreement with the 10 to 14% estimated through the correlation method.

Dustfall deposition velocities have been determined for several elements and the size of the particles associated with these elements has been estimated using an empirically derived Stokes Law approximation based on the fact that Pb particulates have a mass median diameter (mmd) of about $0.5\text{ }\mu\text{m}$. Copper appears to be on relatively large particles, $1.8\text{ }\mu\text{m mmd}$ while nickel and vanadium which are believed to originate as fumes in oil burning sources, have mass median diameters of less than $1\text{ }\mu\text{m}$.

The studies are being extended using a new size selective sampler to determine particle size-composition relationships, and possible interrelationships with human tissue burdens.

Further efforts are being made to refine the data and the computational techniques in order to better assess the source-aerosol and tissue burden-aerosol relationships.

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AIR POLLUTION PROBLEMS IN LATIN AMERICA

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ABSTRACT

Latin America includes 20 countries of different size, socio-economic condition and type of government. The total population is reaching 300,000,000, with 50% rural, but including two of the ten largest cities in the world, with nearly 10,000,000 inhabitants in each.

In the late 50's some measurements of air pollutants were made. In 1967, the Pan American Health Organization started a continental network of sampling stations. The Pan American Network of Air Pollution Monitoring Stations has now 92 stations in 25 cities of 13 countries. By December 1973 it had collected over 300,000 data on particles and sulphur dioxide, which show the magnitude of the problems affecting the main cities. Some of them present monthly averages three or more times higher than the reference levels.

The main air pollution problems seem to be industrial combustions. Motor vehicles, with a total around 10,000,000, are concentrated in the main cities. These, combined with plenty of sunshine, cause a problem in some of them. Home heating is seldom used, and only a small proportion of garbage is incinerated.

An Under-Secretariat for Environmental Protection was established by Mexico in 1972, and by Argentina and Brazil in 1973. A few control programs are at present in operation, and some institutions have been especially created to make air pollution studies. The main deterrent for good air pollution programs is the scarcity of well-trained personnel. Academic and short courses, as well as scholarships and travel grants, are trying to solve this problem.

Research on air pollution is just starting in Latin America. Most of it deals with measurement of air pollutants, but some has been done on health effects, mainly in Chile and Mexico. These studies are still too few in number, but they are showing the right path to the Latin American scientists and those from other developing countries.

Latin America includes 20 countries of very different size, population, socio-economic condition and even type of government. It is difficult to compare the giant Brazil with the tiny El Salvador; a fairly well-developed, industrialized country, like Argentina, with a mainly agricultural one, like Haiti; a socialist country as Cuba, with one with a market economy, as Venezuela; etc. Per capita incomes differ also widely, going from less than US\$ 100 to nearly US\$ 1,200 per year. The environmental problems are also very different. The total population is reaching 300,000,000 including two of the ten largest cities in the world, with nearly 10,000,000 inhabitants each, and 50% of the total as rural population, very disseminated. Air pollution is still incipient, but some of the most important cities, like Mexico City, Buenos Aires, Sao Paulo and others, are quite polluted.

The Latin American governments began to worry about air pollution during the late 50's when some sporadic measurements were made, mainly by universities and occupational health departments. In 1965 the Directing Council of the Pan American Health Organization (PAHO), to which the 20 countries belong, recommended to its Director the initiation of air and water pollution programs, to help the Member Governments in the development of adequate policies. At the end of 1966 a permanent air pollution regional consultant was hired.

Since any good program should start with a thorough knowledge of the magnitude of the problems, PAHO, through its Pan American Center for Sanitary Engineering and Environmental Sciences (CEPIS), decided to initiate a continental network of air pollution sampling stations. It was decided to collect monthly samples of settled dust, by means of a dust jar, and daily samples of suspended dust and sulphur dioxide, measured by the loss of reflectivity of a white filter paper and by the hydrogen peroxide method respectively. A very detailed Manual of Operations was prepared, in Spanish. The Pan American Network of Air Pollution Monitoring Stations (REDPANAIRE) started its operation in June 1967. By the end of that year it had eight stations, and 92 by the end of 1973, covering 25 cities in 13 countries. New others are being added continuously, and it is expected that by 1975 the Network will include most of the Latin American countries and their main cities.

In 1971 a First Report of the Network Results was published analyzing around 40,000 data collected until December 1970. A preliminary version of a Second Report, including 300,000 data collected until December 1973, was published this year, with the final version expected to be ready by July. The analysis of the data shows that several cities in the Network had high results, doubling and tripling in some cases the recommended reference levels. This is especially true for settled dust, with the highest values found in some of the stations of Mexico City, and in Cordoba and Buenos Aires, both in Argentina.

Sao Paulo, Buenos Aires, Mexico, Havana and Rio de Janeiro have the highest values for suspended dust, with figures over three times the reference level. Some cities, like Buenos Aires, show well-defined seasonal variations, and a clear upward trend. Sulphur dioxide concentrations seem to be the worst in Mexico City, Caracas, Santiago and Sao Paulo, with monthly averages three and even four times higher than the reference level.

A comparison between the 1970 and 1973 reports shows important increments for several cities and the clear need to initiate control programs designed to eliminate the damages already occurring and to prevent the appearance of new problems.

Besides the REDPANAIRES measurements, other activities are being developed by several countries. The most important can be found in Mexico City, where a Philips automatic and computerized network of 20 stations, to measure five of the main pollutants, is under installation. This will be an important experience and when under full operation should give a good picture of the situation, guide the Mexican control program, and serve as a training ground for Latin American personnel.

Mention can be also made of the measuring programs in Rio de Janeiro and Sao Paulo. In Caracas, Venezuela, besides eight stations of the REDPANAIRES there is a carbon monoxide detector in operation, and several other instruments are being considered. Colombia, with the most extensive national network of REDPANAIRES type stations, a total of 25 distributed among six cities, intends to expand it and is expecting the arrival of a carbon monoxide detector. Several other cities are planning also to expand their measurement programs.

The main air pollution problems in the Latin American countries seem to be industrial combustion, and in some cases combustion of solid

wastes. Motor vehicles, even if at a low number on the average, with a total of 9,108,400 in 1970, are fairly well concentrated in the main cities, which combined with plenty of sunshine causes a problem in some of them, mainly Mexico City, Sao Paulo, Buenos Aires and Santiago. Due to the hot climate, home heating is seldom used, with the exception of Argentina and Chile, the southernmost countries. Burning of garbage in apartment buildings is usually a problem, due to poor incinerators design, but fortunately there are not too many of them, for the time being, even in the largest cities. Municipal incineration is also a rarity, with Buenos Aires as one of the exceptions.

Better understanding of the magnitude of the problem has moved some of the Latin American Governments to act. An Under-Secretariat for Environmental Protection was established by Mexico in 1972, followed in 1973 by similar institutions in Argentina and Brazil. The Mexican Under-Secretariat has a staff of over 450, more than 50% of them professionals. A basic environmental protection law and a regulation on particles emission have been promulgated, and some control is trying to be applied to the 150,000 factories in the country. However important these efforts, the air pollution problem in Mexico City is perhaps one of the most serious in Latin America.

Control programs are in operation in other countries. Mention can be made of those in Argentina; Rio de Janeiro and Sao Paulo, Brazil; Chile; Colombia; Peru, and Venezuela. Peru, the biggest fisher, and exporter of fishmeal, in the world, with a catch of 12 million tons of anchovy in 1971, its record year, has been fairly successful in the control of odors emitted by the factories surrounding its capital, Lima. Chile and Venezuela have established institutions for air pollution studies, the Institute of Occupational Health and Air Pollution Research in Chile, and the Center for Research on Environmental Pollution in Venezuela. The last one, with the technical support of PAHO and with an important financial aid of the UNDP, is expected to expand air pollution programs in this country.

The most important deterrent to the development of good air pollution programs in the Latin American countries is the scarcity of well-trained personnel. PAHO is helping to correct this by giving technical assistance in the preparation of programs, legislation, regulations, etc.,

and for the solution of specific problems. Seventeen countries have benefited from this activity. Assistance has been also given to the universities for the development of air pollution courses, like those in Argentina, Brazil, Chile, Colombia, Mexico and Venezuela. Seven short courses on air pollution have been presented in five countries, as well as lectures at other 24 short courses and seminars. In 1968, a Latin American Seminar on Air Pollution was held in Rio de Janeiro, with delegates from eight countries. The information collected at this opportunity, and later published, is still the best and more complete available. PAHO, through its Fellowship Program, has also assigned scholarships and travel grants.

Research on air pollution is just starting in Latin America, and all the work being done is of the applied type. Most of it deals with measurements aimed at the establishment of the real magnitude of the problems. Besides the activities of REDPANAIRE and other measurement programs, work on concentration of specific pollutants has been done in at least eight countries. Mexico and Peru have dealt with the efficiency of the measuring methods.

Some research has been done on the health effects of air pollutants. The Institute of Occupational Health and Air Pollution Research of Chile has published at least three papers. One dealt with concentration of carboxihemoglobin in the blood of people exposed to carbon monoxide. The second one makes a comparison of several clinical and physiological characteristics of a group of people from Santiago, the capital, with another from a rural town, supposedly non-exposed. The last one made a study of the effect on children of airborne pesticides. Mexico prepared one of the most extensive studies, looking for a correlation between the results of the REDPANAIRE stations and clinical and physiological observations made on inhabitants of Mexico City. Even if these studies are still in their preliminar stage, and are too few in number, they are showing the right path for the Latin American scientists, and those from other developing countries, to get a real knowledge of their own problems.

PANEL DISCUSSION

SUMMARY OF THE DISCUSSION

SYROTA (France)

La table ronde débute par cinq exposés traitant tous de techniques de mesure ou d'analyse de polluants atmosphériques.

Pour estimer sur un site donné quelle était la répartition des concentrations de polluants dans le passé, M. English propose diverses techniques qui interpolent ou extrapolent les rares mesures disponibles:

- l'utilisation de modèles de qualité de l'air;
- l'utilisation des données de production;
- la construction de courbes d'égale concentration, par interpolation linéaire des mesures disponibles;
- l'emploi d'indicateurs de pollution, pour estimer à partir des retombées connues d'un polluant celles d'un autre.

M. Lauer présente le programme CHAMP de l'EPA qui vise à acquérir des données sur la qualité de l'air, afin d'évaluer l'influence des polluants sur la santé de cinq communautés américaines (programme CHES). Il comprend 23 stations de mesure situées dans cinq zones géographiques. Tout est continuellement contrôlé grâce à un mini-ordinateur: calibrage, analyse et validité des données, ainsi que fiabilité des stations et des appareils de mesure.

M. Dams a évalué les niveaux d'empoussiérage en Belgique. Toutes les particules en suspension ont été recueillies sur des filtres de cellulose pendant un an dans 14 sites industriels, urbains et ruraux, puis analysés par activation électronique, absorption atomique et gravimétrie. Les sources d'émission importantes peuvent en particulier être localisées en comparant les compositions chimiques élémentaires des particules collectées sur un ou plusieurs sites, mais sous différentes directions de vent.

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M. Kneip montre que, grâce à l'analyse et aux compositions des aérosols recueillis à New-York, les éléments les plus caractéristiques à l'état de traces qui peuvent être associés à des sources urbaines sont: le plomb, le vanadium, le cuivre, le sodium et le potassium. L'importance de leur absorption par les new-yorkais est étudiée à partir des retombées de particules, de leur dimension, de leur vitesse de déposition et de leurs traces dans les tissus humains.

M. Vouk fait le point sur la pollution de l'air en Amérique Latine. Depuis 1967, la Pan American Health Organisation (PAHO) a établi un réseau de mesure qui comprend actuellement 92 stations dans 25 villes de 13 pays et qui mesure le SO_2 (par la méthode à l'eau oxygénée) et les particules en suspension (par réflectométrie). Les principales sources de pollution sont les combustions industrielles et le problème le plus préoccupant reste le manque de personnel qualifié. Des études épidémiologiques sont en cours.

La discussion qui s'ouvre alors porte principalement sur les analyses et les résultats obtenus par l'équipe de M. Kneip, sur le coût d'un réseau de mesure sur la validité des données collectées par la PAHO et sur les mesures de particules de sulfates qui semblent mieux corrélées avec les effets sur la santé que le SO_2 .

Mais le véritable objet de la table ronde - qui n'était pas de donner des détails sur les systèmes de mesure existants, mais de discuter sur la manière dont ces systèmes peuvent être utilisés pour mesurer l'exposition des personnes aux polluants de l'air - n'est abordé au cours du débat que par MM. Vouk et Sherwood. Puisque les mesures effectuées à partir d'installations fixes semblent ne pas fournir de données appropriées, parce que d'une part la population surveillée se déplace souvent et d'autre part les appareils ne sont pas forcément établis dans les endroits où la population est exposée aux plus fortes pollutions, le port de petits compteurs individuels de genre de ceux qui

sont utilisés pour évaluer la contamination radioactive des personnes, est suggéré. Mais cette méthode assez pertinente semble avoir rencontré certaines difficultés à l'EPA qui a annulé ses essais récemment.

The discussion began with five statements dealing with techniques for measuring or analysing atmospheric pollutants.

As a means of estimating what the distribution of pollutant concentrations have been in the past on a given site, Mr. English suggested various techniques for interpolating or extrapolating the few measurements actually available;

- use of models of air quality;*
- use of production data; construction of equal-concentration curves by linear interpolation of the available measurements;*
- use of pollution indicators to predict the immission of a given pollutant on the basis of the known immission of another.*

Mr. Lauer introduced the EPA's CHAMP programme, the aim of which was to obtain data on the quality of air so as to determine the effects that pollutants had on the health of five American communities (CHESS programme). There were 23 measuring stations in five geographical areas and everything was monitored continuously by means of a mini-computer; calibration, analysis and validity of data, as well as the reliability of the measuring stations and equipment.

Mr. Dams said he had studied dust levels in Belgium. All the particles in suspension were collected on cellulose filters for a year at 14 industrial, urban and rural sites, then analysed by electronic activation, atomic absorption and gravimetry. The chief emission sources in particular could be located by comparing the elementary chemical composition of particles collected at one or more sites and correlated with wind direction, which should be variable.

Mr. Kneip showed that, from the analysis and the composition of the aerosols collected at New York, the most typical elements in the form of traces which could be associated with urban sources were lead, vanadium, copper, sodium and potassium. The extent to which they were absorbed by New Yorkers was studied on the basis of the immission of the particles, their size, rate of deposition and the trace quantities of them present in human tissue.

Mr. Vouk spoke of air pollution in Latin America. Since 1967 the Pan American Health Organisation (PAHO) had set up a measuring network which currently comprised 92 stations in 25 towns in 13 countries. Sulphur dioxide was measured by the hydrogen peroxide method, and the particles in suspension by reflectometry. The main sources of pollution were industrial combustion processes, and the problem giving rise to most concern was still the lack of qualified staff. Epidemiological studies were currently in progress.

The main topics of the discussion which followed were the analyses carried out by Mr. Kneip's team and the results obtained on the cost of a measuring network, the validity of the data gathered by the PAHO, and measurements of sulphate particles which seemed better correlated with the effects on health than was sulphur dioxide.

However, the true purpose of the panel discussion was not to go into the details of existing measuring systems, but to examine the ways in which such systems might be used for measuring human exposure to air pollutants, and that had been dealt with during the debate only by Mr. Vouk and Mr. Sherwood. It appeared that measurements taken at fixed measuring stations did not provide the appropriate information. That was due partly to the fact that the measuring equipment was not necessarily located at the points where the population was exposed to the greatest pollution. The wearing of small personal counters of the type used to assess the radioactive contamination of human beings was suggested, but although the method was certainly appropriate, the EPA had apparently encountered certain problems with it, and had recently suspended its testing.

DISCUSSION

SYROTA (France)

Cette table ronde a pour titre: la mesure de l'exposition à la pollution atmosphérique. Il s'agit là d'un problème particulièrement important et difficile.

La mesure est à la base de toute étude scientifique. Il est pourtant malaisé de faire admettre cela, dans le domaine de la pollution atmosphérique, puisqu'il n'existe pas, à ce jour, de

méthode de référence, d'étalon si vous voulez, même pour les polluants les plus répandus, si bien que l'utilisation des connaissances acquises dans le monde sur les effets de différents polluants sur la santé ne peut donner que des résultats contestables. La mesure porte en effet sur des traces, des concentrations de l'ordre de milliardièmes, et tout résultat est influencé par l'effet d'autres polluants, qui, du reste, ne sont pas toujours les mêmes.

Il existe néanmoins, depuis quelques années, de nombreux réseaux de mesure, permanents ou non, dans le monde, probablement plusieurs milliers d'appareils et les questions que l'on peut se poser consistent à savoir s'ils existent depuis suffisamment de temps pour que l'on puisse en déduire d'importance des doses absorbées par la population et s'ils donnent effectivement des indications en rapport avec l'exposition de la population. Autrement dit, connaît-on la structure, la composition et l'implantation idéales d'un réseau de mesure destiné à évaluer l'exposition de la population?

Il faut se souvenir que l'on a affaire à une population variée, qui comprend des enfants, des adultes, des vieillards, chacun pouvant être malade ou en bonne santé, travailler ou non, se déplacer peu ou continuellement pendant une partie de la journée. L'essentiel des mesures concerne actuellement l'air ambiant et les atmosphères de travail.

Dans ce dernier cas, les problèmes sont relativement simples, les concentrations maximales admissibles sont souvent définies et, dans l'ensemble, peu contestées. Dans l'air ambiant, on s'intéresse à des concentrations qui sont souvent cent fois plus faibles et on ne peut définir de teneurs limites puisque le but affiché de tous les gouvernements est de protéger l'ensemble de la population sans exception. Rien n'empêche en effet de penser que la concentration en polluants susceptible de troubler davantage la santé du citoyen marginal dont l'état sanitaire est le plus dégradé, soit particulièrement faible.

Dans l'air ambiant, souvent, les réseaux de mesure mis en place servent à indiquer surtout l'évolution de la pollution dans le temps, là où elle est déjà relativement élevée et à contrôler les installations les plus polluantes. Les polluants mesurés sont alors les meilleurs traceurs de la pollution surveillée comme par exemple le dioxyde de soufre pour la combustion ou le monoxyde de carbone pour les véhicules, sans qu'ils soient forcément ceux qui entraînent des effets nocifs sur la population.

D'ailleurs la lumière n'est pas faite sur la nature, la forme, l'état et les dimensions, des polluants qui, directement ou indirectement entraînent des effets nocifs sur la santé. Les phénomènes de synergie qui interviennent à coup sûr et les corrélations entre la durée d'exposition et les risques encourus sont encore mal connus. Ceci incite tout naturellement à effectuer des mesures très nombreuses.

Les recherches deviennent alors complexes et mettent en jeu des compilations énormes de données: il suffit de peu de capteurs et de peu de semaines pour se retrouver à la tête de millions de résultats de mesure.

Lorsque l'on s'intéresse à l'exposition, il faut disposer de capteurs dont on puisse théoriquement intégrer les résultats en fonction des déplacements de la population. C'est une entreprise ardue: comment, en effet, connaître les effets de la pollution due aux automobiles? Au milieu des rues où la circulation est intense, on trouve des dizaines de parties par million de polluants, sur le trottoir on n'en trouve plus que la moitié, et dans les rues plus calmes on n'en trouve plus que des traces. Combien de temps passe-t-on dans les rues les plus polluées? De même, comment tenir compte de la pollution à l'intérieur des locaux d'habitation? Certes, une partie de cette pollution provient de l'extérieur, mais s'intéresse-t-on assez aux polluants émis dans le logement, par exemple par les cuisinières à gaz, par les fours autonettoyants ou par les installations de chauffage individuelles?

Voilà, brièvement tracé, le décor, pas très rose, dans lequel se place cette table ronde. Ayant entendu les exposés introductifs la discussion est maintenant ouverte.

The title of this round table conference is 'The measurement of exposure to atmospheric pollution'. This is a particularly important and difficult problem.

Measurement is at the basis of all scientific study. In the field of atmospheric pollution, however, it is not easy to persuade people that this is so, since there is at present no method of reference, no standard, even for the most common pollutants, which means that the use of the knowledge acquired throughout the world on the effects of various pollutants on health can produce only questionable results. Measurements are being made on mere traces, concentrations of the order of one thousand millionth part, and any result is influenced by the effect of other pollutants, which, moreover, are not always the same.

Nevertheless, for some years now numerous measurement networks, permanent or temporary, have been in operation in all parts of the world, probably comprising several thousand instruments, and the question may be asked whether they have been in existence long enough to enable the volume of intakes absorbed by the population to be deduced and whether they in fact provide consistent information regarding the exposure of the population. In other words, do we know the ideal structure, make-up and layout in space of a measurement network intended to evaluate the exposure of the population?

We must remember that we are dealing with a varied population, which includes children, adults and old persons, each of whom may or may not be in good health, may or may not work, may travel little or extensively during part of the day. At the moment most measurements are carried out on the outside ambient air and on the atmosphere of work places.

In the case of the latter, the problems are relatively simple, since maximum allowable concentrations are generally well-defined and on the whole give rise to little controversy. As regards the outside ambient atmosphere, interest centres on concentrations which are often a hundred times lower, and it is not possible to establish threshold limits, since the avowed aim of all governments is to protect the population as a whole, without exception. One cannot help believing that the concentration of pollutants which is likely to affect the health of citizens living on the fringe of society, whose physical condition is particularly poor, is especially low.

In the case of the ambient air, the measurement networks installed are often intended to indicate, above all, trends of pollution over a certain period of time, in cases where it is already relatively severe, and to monitor the most highly polluting installations. The pollutants measured then are those providing the best indication of the pollution monitored, such as sulphur dioxide in the case of combustion or carbon monoxide in that of motor vehicles, but not necessarily those which have harmful effects on the population.

Moreover, much light remains to be shed on the nature, form, state and dimensions of the pollutants which, directly or indirectly, have harmful effects on health. The synergistic processes which inevitably occur and the correlations between the length of exposure and resulting hazards are as yet little known. The natural consequence is that large numbers of measurements are taken.

Research then becomes complex and involves the compilation of enormous amounts of data; in the space of a few weeks, a few monitoring devices can produce millions of measurements.

In order to measure exposure, it is necessary to have monitoring devices, the results of which may theoretically be integrated according to population movements. This is a most difficult task, for how can one determine the effects of pollution from motor cars? In streets where traffic is heavy, pollutants are present in dozens of parts per million, but at the pavement this amount is halved and in quieter streets only traces can be found. How much time do people spend in the most polluted streets? Similarly, how can one allow for pollution in dwellings? True, some of this pollution comes from outside, but is enough attention paid to pollutants emitted inside the dwelling, by gas cookers for example, self-cleaning ovens or individual heating installations?

This, then, is the setting, and not a very rosy one, for this round table conference. Now that the introductory talks are over, the discussion can be opened.

KNEIP (U.S.A.)

I think I can immediately see one distinguishing feature between our studies and the studies that we have just heard about from the panel members. All three that we have heard are very large government supported programmes, ours is a study being performed at a private university supported by the American Petroleum Institute and the Electric Power Research Institute.

Our approach has been to attempt to understand some of the composition relationships in the urban aerosol through a program which could be handled by a small group in terms of number of samples and analyses to be performed. Despite the fact that our group numbers only five people, we have been able, by use of the weekly sampling technique noted in our paper, to effectively define a number of the relationships affecting both the concentration and composition of the total suspended particulate matter in the New York City air. While the larger programs may be highly productive, carefully planned efforts with well-defined objectives may be carried out quite well by such a small group as ours.

In addition to the relations reported in our paper, we have recently accumulated enough data on tissue analysis to begin analyzing and correlating these results. We found that along with the reduction of lead in air, we have a reduction of lead in lung tissue of the people in the city as represented by our sample, and in fact we have a very strong linear correlation between the two.

VOUK (W.H.O.)

As has already been pointed out, the purpose of this panel is not to discuss various details of the existing air pollution monitoring systems but rather to exchange views with the audience, as to what extent monitoring systems, designed for other purposes such as checking the implementation of regulations or standards, or for evaluating the effectiveness of control measures, can be used for assessing human exposure. Obviously, levels of air pollutants should not be identified with the true exposure of an individual or population group. Since exposure has been defined as the amount of a pollutant reaching the target (i.e. man or, to be more precise, his respiratory system) under specified conditions (i.e. concentration, frequency of exposure and its duration), I hoped that questions from the audience would help us to clarify some of the aspects of the design of air quality monitoring systems for assessing human exposure. For instance, how should such a system be designed, are fixed sampling stations

adequate for measuring human exposure, or should we perhaps aim at personal monitoring equipment, similar to that used sometimes in industrial hygiene or, more frequently, in radiological protection?

Reference was made to Mr. Haddad's paper, not because it describes an air pollution monitoring system which has been designed to measure human exposure, but because it was one of the first attempts to collect, on an international basis, information on basic air pollution data in a number of Latin American countries that will allow a comparative study of the situation in the cities included in the network and help to determine the trend of the problem; also, because it will awaken greater interest in the participating countries in air pollution problems and help them to set up a well-organized administrative structure with trained personnel for air pollution control. The Pan-American Air Pollution Monitoring Network, described in Mr. Haddad's paper, was initiated in 1967 and by December 1973 there were 93 monitoring stations located in 26 cities in 14 countries. The air quality variables generally measured include settled dust (monthly average), suspended dust (daily average) and sulfur dioxide (daily average). This activity, initiated by the Regional Office of WHO for the American and the Pan-American Health Organization is a part of the WHO air pollution monitoring programme which, in addition to Latin America, includes 13 Member States with three monitoring stations in each of them. The Pan-American Air pollution Monitoring Network has not yet been completely integrated with WHO activities in other countries built is planned to do so in the near future.

BRAVO (Mexico)

I would like to comment as to the validity of the data that has been collected by the PAHO network in Latin America. Mr. Lauer has stressed the importance of valid measurement technique yet the PAHO network measured suspended particles using the

reflectance method to report $\mu\text{g}/\text{m}^3$. This method is based on standard smoke curve - developed in England and since we have no heating by coal it does not apply to our estimation of total suspended particles. The data obtained is not useful for control strategies design.

VOUK (W.H.O.)

I would like to answer this question very briefly. Of course, the measurement of suspended particles using the reflectance method, developed originally in England and adopted by the OECD, is not the ideal method to be applied in Latin American countries. However, the purpose of the Pan-American Air Pollution Monitoring Network has not been to obtain absolute values for suspended particulate matter in air but to follow the trends, and for this purpose I think the method is good enough. It may be mentioned in passing that none of the existing routine methods for measuring suspended particulate matter are satisfactory. High-volume sampler results are also not comparable if obtained in different conditions because the particle size distribution will greatly influence the results. In addition, if we want to use the index of suspended particulate matter for evaluating exposure/effect relationships for man, a detailed chemical analysis of the sample is required in addition to the particle size distribution. This is in fact the major problem in all epidemiological studies performed so far. When one of the WHO Expert Committees which met in 1972 in Geneva was asked to propose criteria for particulated and sulfur dioxide it found that a large proportion, almost 90 per cent, of the available epidemiological information had to be discarded because the exposure measurements were not comparable. The criteria for suspended particulates and sulfur dioxide which were published in WHO Technical Reports Series No. 506 refer actually to the smoke shade method, not because this method is recommended, but because the only information that seemed to be valid was obtained by measuring exposure to suspended particulate matter using this method.

Of course, we need also better methods for the design of control strategies, but here again the choice has to be left to the countries. The WHO has prepared and will publish soon a Manual on Selected Methods for Sampling and Measuring Urban Air Pollutants. This manual proposes for each pollutant several methods which are applicable under certain conditions and also for each pollutant a single "comparison" method, by which the methods routinely used in different countries can be calibrated and compared, at least approximately.

PHAM (France)

A combien peut-on estimer le coût pécunier et le nombre de personnel pour une organisation de mesures, comme celle présentée par M. English?

What is the cost and the personnel requirements for a measuring network as that presented by Dr. English?

ENGLISH (U.S.A.)

To give you a rough idea, consider the regional air pollution study in St. Louis. That study is a five year program involving 25 very complete air monitoring stations which measure essentially all pollutants and meteorological parameters. The study includes gathering data not only from ground stations but also from airborne platforms such as 3 helicopters and 11 fixed-wing aircraft. It includes a meteorological sounding network to determine the three dimensional temperature and wind velocity distribution. It also includes a modeling effort to compare the results which are obtained through the measurements with those predicted through a variety of air pollution meteorological models. The price of this programme is roughly 25 million dollars, 5 million dollars per year for five years.

WESOLOWSKI (U.S.A.)

How close together must the monitoring stations be in an area such as the Los Angeles Basin, where physical and Chemical kinetics are an extremely important component of the pollution problem, in order for the isopleth model you described to be truly useful?

ENGLISH (U.S.A.)

Isopleths estimate concentrations of a pollutant at locations where the pollutant has not been measured. These estimates can be performed in many different ways which produce identical results at the air monitoring stations. For example, you can weigh the values obtained at each air monitoring station using the inverse square of the distance from the location in question to each station. This is a popular approach. Others prefer to use a direct inverse relationship. Neither of these approaches has any sound physical justification for its use. The relationships which I have presented are based on the criteria of simplicity. The simplest approach that reproduces the multiple station data set at the station locations, and estimates the values between stations is linear interpolation. In order to estimate the error in this approach, we made some concentration estimates for the Los Angeles area in which individual stations were left out of the analysis. This produced changes that were quite small, for example approximately 20%.

SHERWOOD (U.K.)

Occupational Hygiene has demonstrated that there is seldom any relationship between fixed position air samplers and exposure of workers. Why therefore should fixed position samplers in cities represent exposure of any of its inhabitants? An example is quoted of the use of a personal SO_2 sampler in London that

showed very wide variation of concentration depending on location of the individual, and raised questions of the biological significance of short-term peak concentrations. There is need for better estimation of exposure of individuals in cities and elsewhere.

ENGLISH (U.S.A.)

We agree quite strongly with the need for personal environmental monitors. We have had a task force in the Environmental Protection Agency looking into the feasibilities of such monitors and they do appear to be feasible. One other comment, the usefulness of past exposure estimates must be looked at in the frame-work of the CHES (Community Health Environmental Surveillance System) programme. The CHES programme selects communities within which the epidemiological studies take place to cover a wide range of pollutant concentrations. For example if three socio-economically comparable communities are studied to determine the health effects of a predominate pollutant, one community will have high concentrations, one moderate and one low concentrations. Within this kind of frame-work one can make useful estimates of past exposures.

STEENBERG (Denmark)

We should be cautious not to be caught by "measurement euphoria". Refined monitoring systems are needed in some parts of the world also for research purposes. But our knowledge of the health implications cannot follow the technical refinements in measurement technique. We have at this symposium had two contributions dealing with particulate sulfates which seem to correlate better than SO_2 and total suspended particulates with health effects. Is WHO undertaking studies to see whether this parameter should be included in more routine monitoring alongside SO_2 and particulates?

VOUK (W.H.O.)

Yes indeed. Among the methods which the World Health organization is now examining for routine air pollution measurements and for comparison purposes is also a method for measuring sulfuric acid aerosols and sulphate particles. It seems, however, that we shall not be able to recommend a satisfactory method very soon and that more research will be needed to develop an adequate method. One of our collaborating institutions is at the moment studying this problem.

KNEIP (U.S.A.)

I would like to comment on this sulphate problem. There has been a long-term study of the relationship of SO_2 and mortality in New York City. It was originally published about 1972 by Goldberg and Schimmel, and Schimmel is in the process of republishing it with an additional set of data. I believe he is now covering 5 to 7 years of mortality data still showing a very strong correlation between variations in SO_2 and variations in mortality from health records in New York City. However, during the period of time involved, the SO_2 level in the city has been reduced by a substantial amount, a factor of 4 or more, but the mortality rate has not decreased. Thus, in all of these cases when we are talking about monitoring and comparing to exposures of the public, and we find a correlation, it should be made absolutely clear that such a correlation does not constitute a demonstration of a cause and effect relationship. If the SO_2 correlation that Schimmel finds represented a cause and effect relationship, the mortality should have decreased when the SO_2 decreased. It did not.

The sulphate has to be looked at the same way. This is a mathematical correlation, it does not prove that sulphate is doing anything having to do with human health although it may be an index or an indicator. Someone has to get behind it and find out why the relationship exists.

VERZEICHNIS

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